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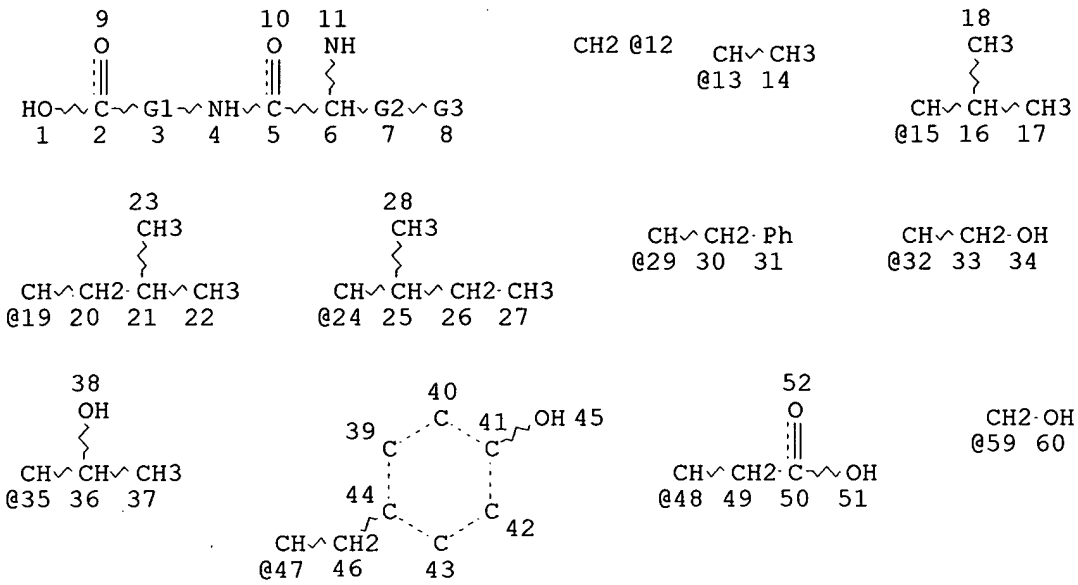
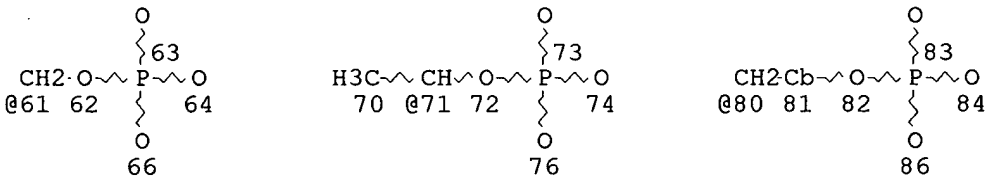


Page 1-A



Page 2-A
VAR G1=12/13/15/19/24/29/32/35/47/48/53
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VAR G3=59/61/68/77/71/80
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CONNECT IS E1 RC AT 84
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CONNECT IS E1 RC AT 86
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 78
GGCAT IS MCY UNS AT 81

DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:
RSPEC 39
NUMBER OF NODES IS 86

STEREO ATTRIBUTES: NONE
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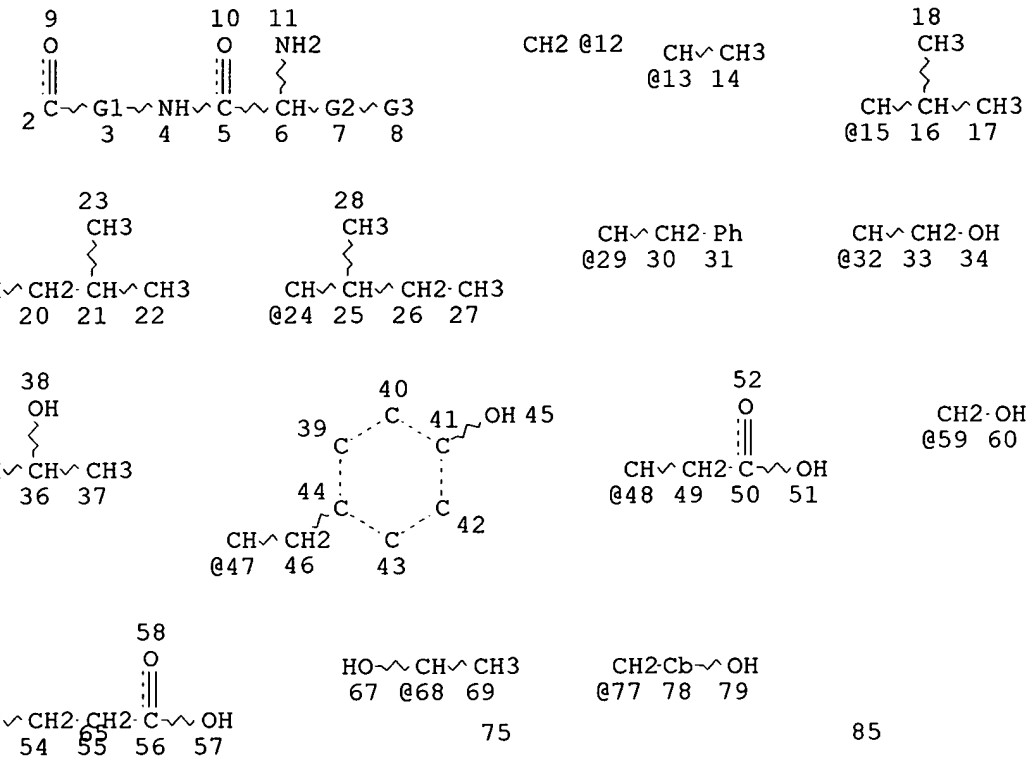

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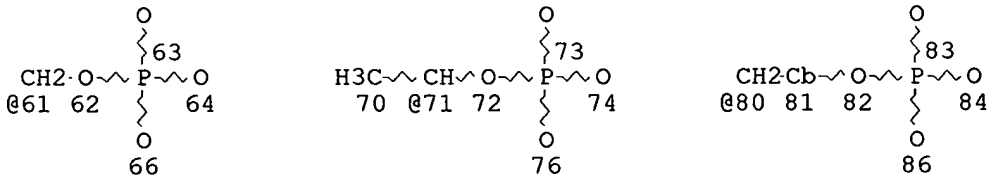

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VAR G3=59/61/68/77/71/80
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GGCAT   IS MCY  UNS  AT  78
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ECOUNT  IS E6 C  AT  78
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GRAPH ATTRIBUTES:
RSPEC  39
NUMBER OF NODES IS  85

STEREO ATTRIBUTES: NONE
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L14               STR
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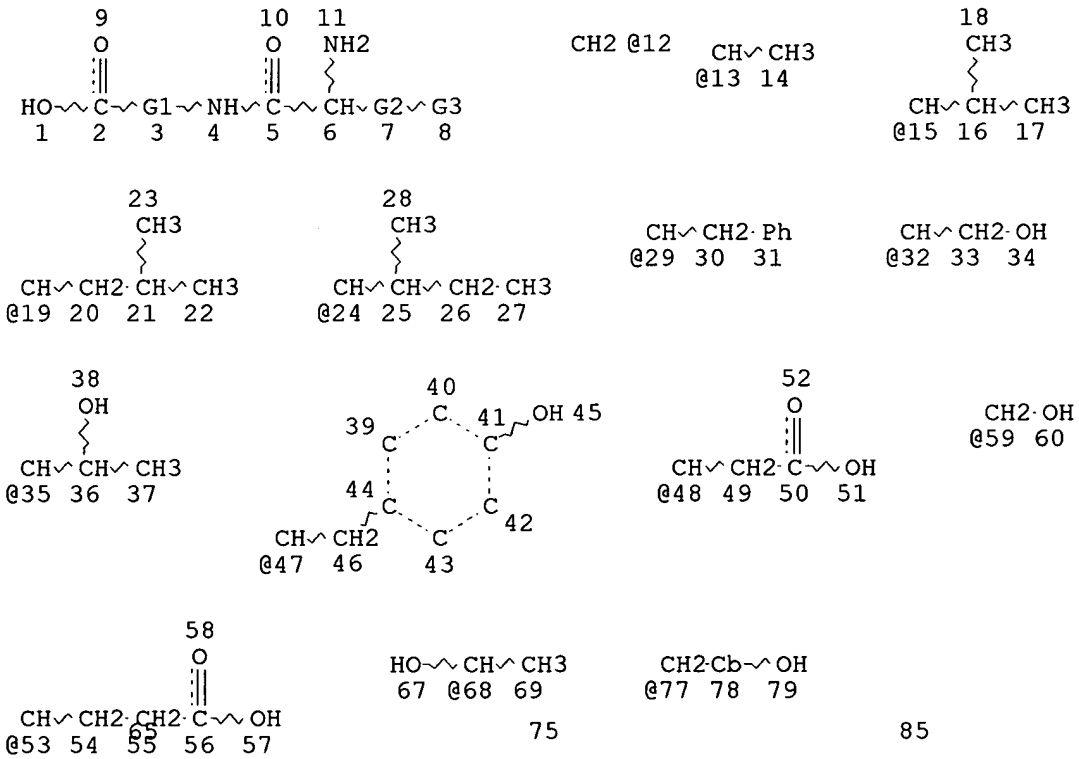

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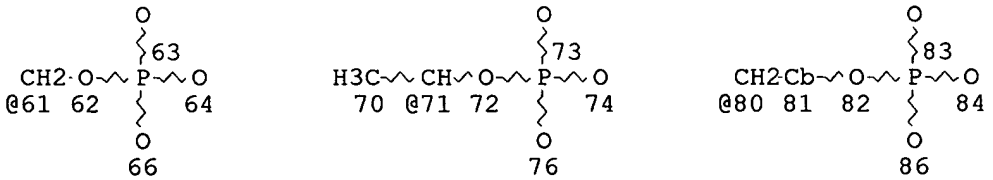

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VAR G1=12/13/15/19/24/29/32/35/47/48/53
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VAR G3=59/61/68/77/71/80
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CONNECT IS E1  RC AT  84
CONNECT IS E1  RC AT  85
CONNECT IS E1  RC AT  86
DEFAULT MLEVEL IS ATOM
GGCAT   IS MCY  UNS  AT  78
GGCAT   IS MCY  UNS  AT  81
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E6 C  AT  78
ECOUNT  IS E6 C  AT  81

GRAPH ATTRIBUTES:
RSPEC  39
NUMBER OF NODES IS  86

STEREO ATTRIBUTES: NONE
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L16             STR
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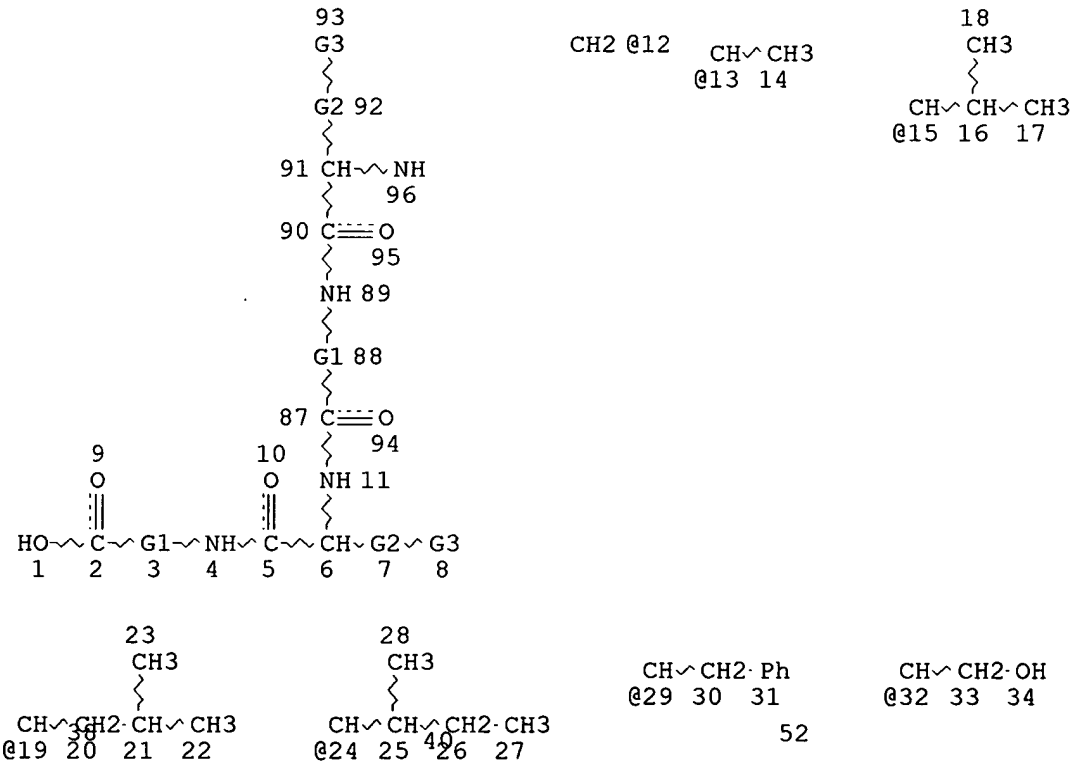
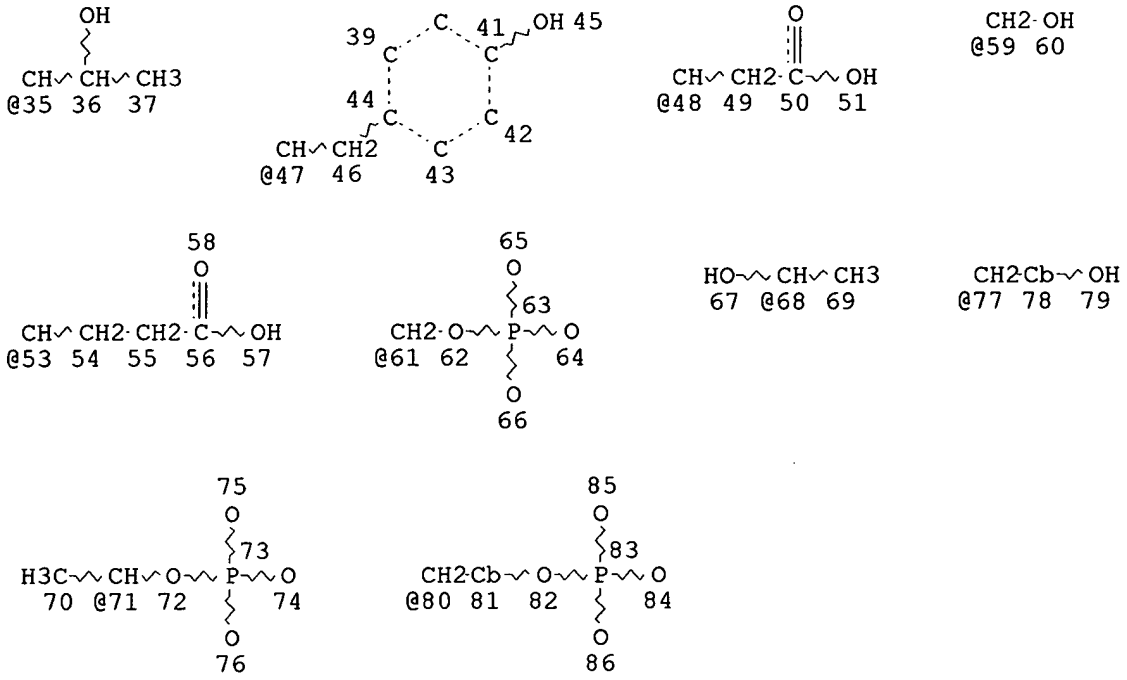


Page 1-A



Page 2-A
VAR G1=12/13/15/19/24/29/32/35/47/48/53
REP G2=(0-10) CH2
VAR G3=59/61/68/77/71/80
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 64
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CONNECT IS E1 RC AT 84
CONNECT IS E1 RC AT 85
CONNECT IS E1 RC AT 86
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 78
GGCAT IS MCY UNS AT 81
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E6 C AT 78
ECOUNT IS E6 C AT 81

GRAPH ATTRIBUTES:
RSPEC 39
NUMBER OF NODES IS 96

STEREO ATTRIBUTES: NONE
L17 10 SEA FILE=REGISTRY SUB=L6 SSS FUL L16
L18 29 SEA FILE=REGISTRY ABB=ON PLU=ON L15 OR L17
L19 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

=> d ibib ab hitstr l19 1-24

L19 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:772123 HCAPLUS
DOCUMENT NUMBER: 135:313632
TITLE: Phosphopeptides and methods of treating bone diseases
INVENTOR(S): Kumagai, Yoshinari; Otaka, Akira
PATENT ASSIGNEE(S): Big Bear Bio, Inc., USA
SOURCE: U.S., 16 pp., Cont.-in-part of U.S. 5,837,674.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6306822	B1	20011023	US 1998-193214	19981116
US 5837674	A	19981117	US 1996-675031	19960703
CA 2258661	AA	19980108	CA 1997-2258661	19970630

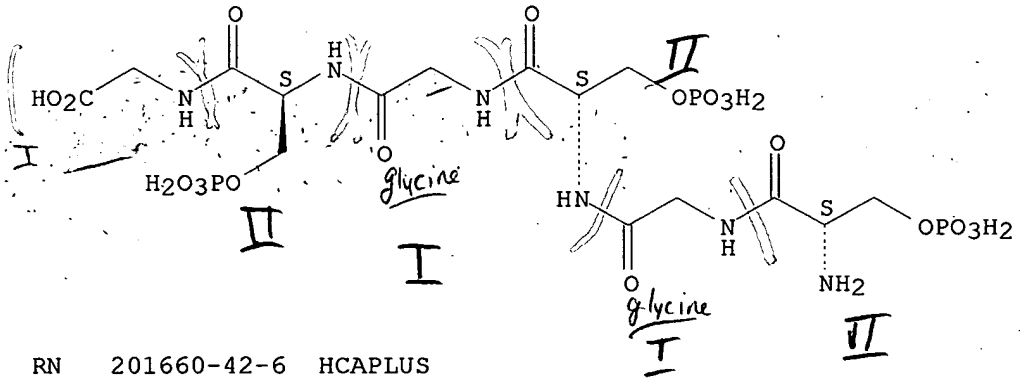
PRIORITY APPLN. INFO.: US 1996-675031 A2 19960703

AB Phosphopeptides which significantly reduce bone loss or weakening are provided by the invention. Also provided is a method for treating or preventing any condition assocd. with bone loss or weakening by administering the phosphopeptides by oral or injectable means.

IT **201660-41-5 201660-42-6 201660-43-7**
328896-68-0 328896-69-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphopeptides and use in bone disease treatment)

RN 201660-41-5 HCAPLUS
CN Glycine, O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

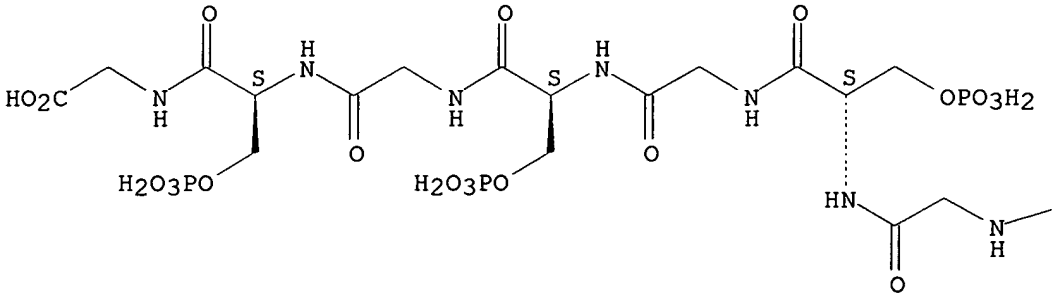
Absolute stereochemistry.



RN 201660-42-6 HCAPLUS
CN Glycine, O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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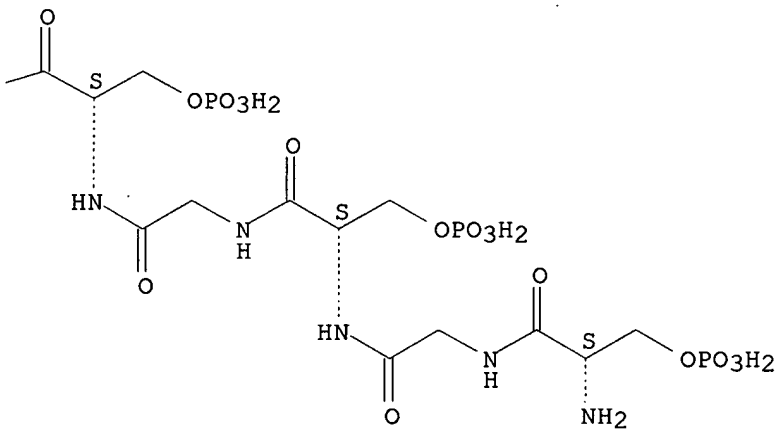
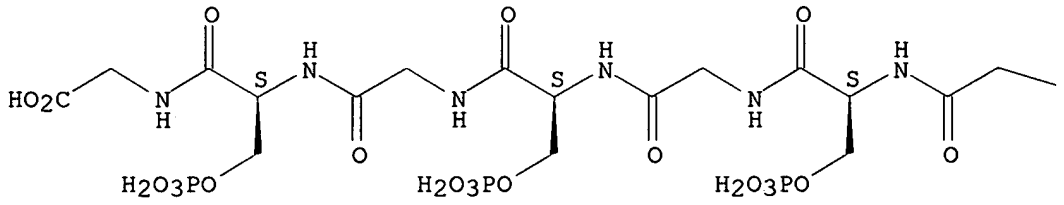


RN 201660-43-7 HCAPLUS
CN Glycine, O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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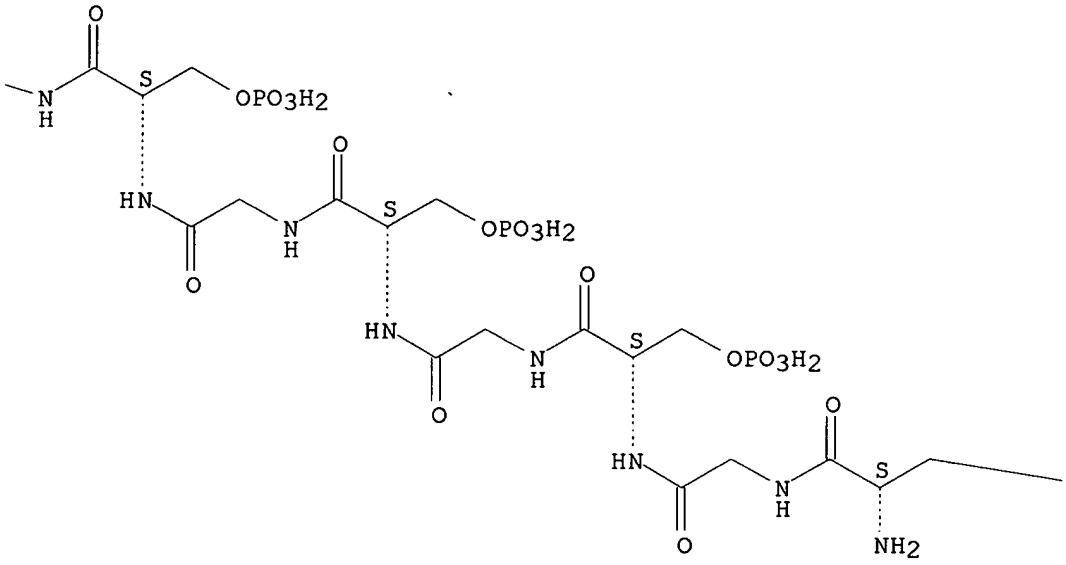


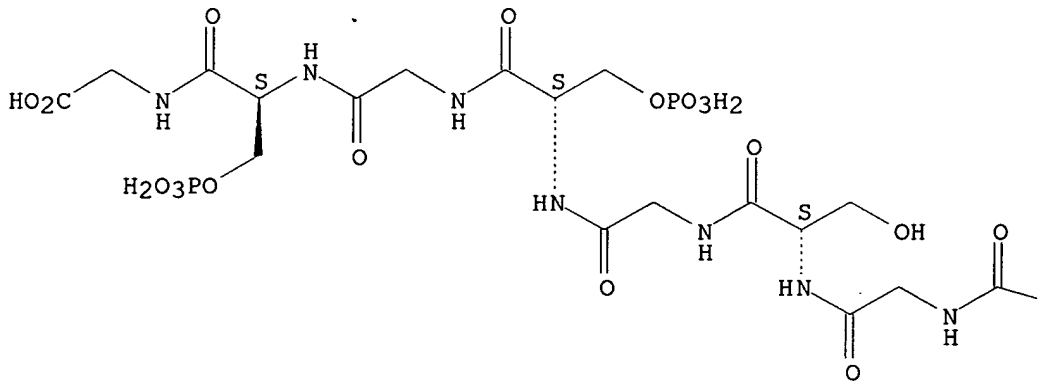
PAGE 1-C

—OPO_3H_2

RN 328896-68-0 HCAPLUS
CN Glycine, L-serylglycyl-L-serylglycyl-L-serylglycyl-L-serylglycyl-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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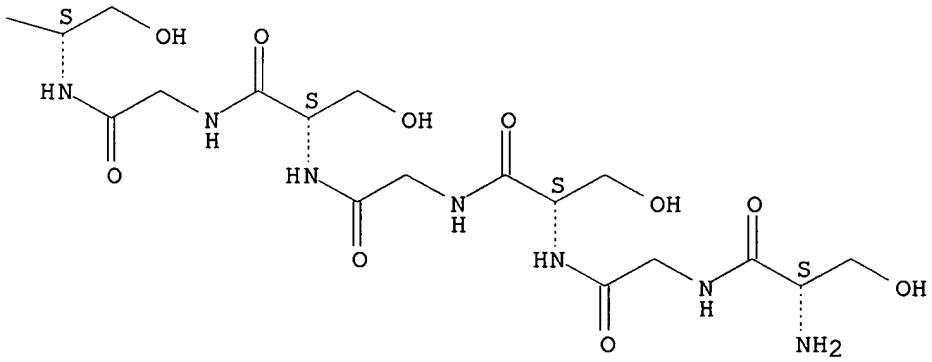
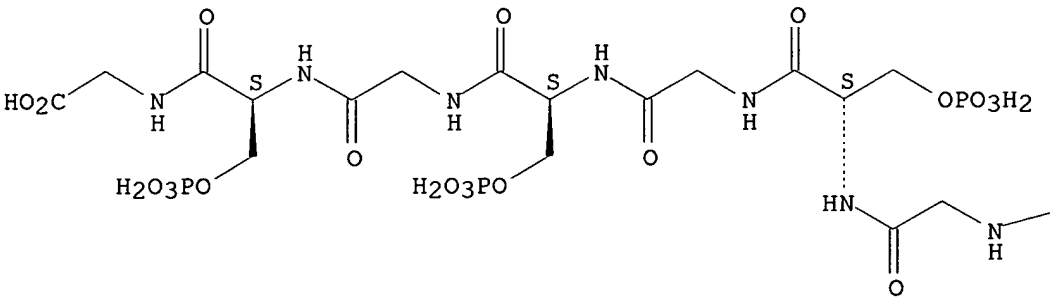


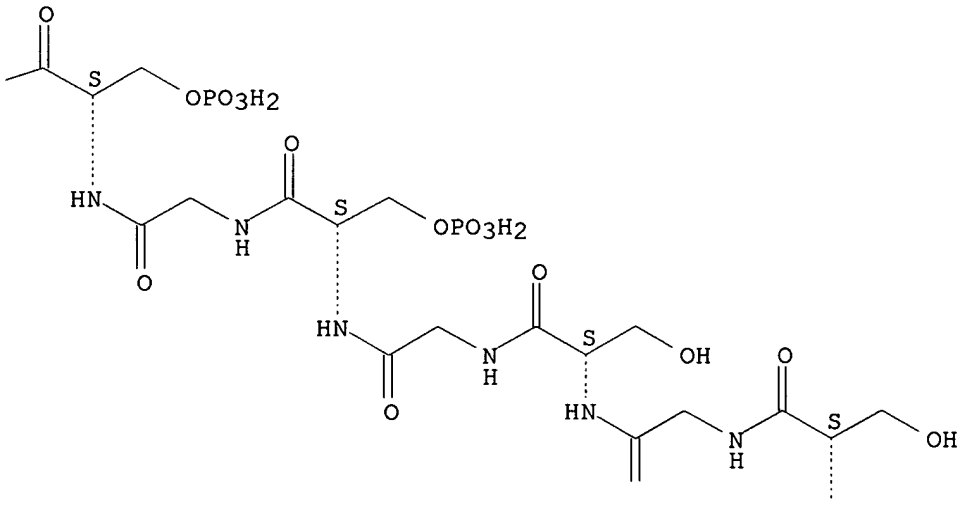
RN 328896-69-1 HCAPLUS
CN Glycine, L-serylglycyl-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-B

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:167827 HCAPLUS
DOCUMENT NUMBER: 134:202705
TITLE: Methods and compositions using peptidic compounds for reducing serum phosphate levels

INVENTOR(S): Kumagai, Yoshinari; Otaka, Akira
PATENT ASSIGNEE(S): Big Bear Bio Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015720	A1	20010308	WO 2000-US22910	20000817
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1207896	A1	20020529	EP 2000-957624	20000817
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-152046P P 19990902
WO 2000-US22910 W 20000817
OTHER SOURCE(S): MARPAT 134:202705

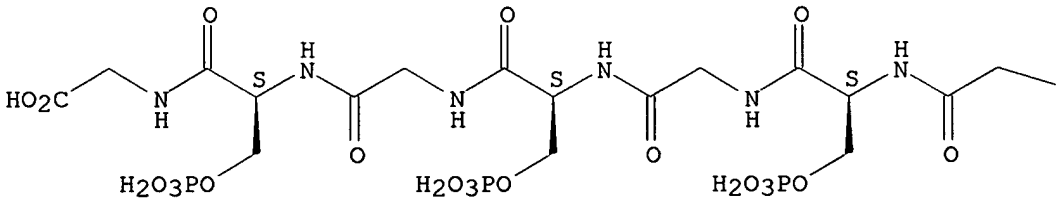
AB Peptidic compds. are provided which significantly reduce serum phosphate levels, and which, in addn., reduce bone loss or weakening. Also provided is a method for treating or preventing any condition assocd. with elevated serum phosphate levels by administering the peptidic compds. by oral or injectable means.

IT **201660-43-7 328896-68-0 328896-69-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidic compds. for reducing serum phosphate levels and reducing bone loss and weakening)

RN 201660-43-7 HCAPLUS
CN Glycine, O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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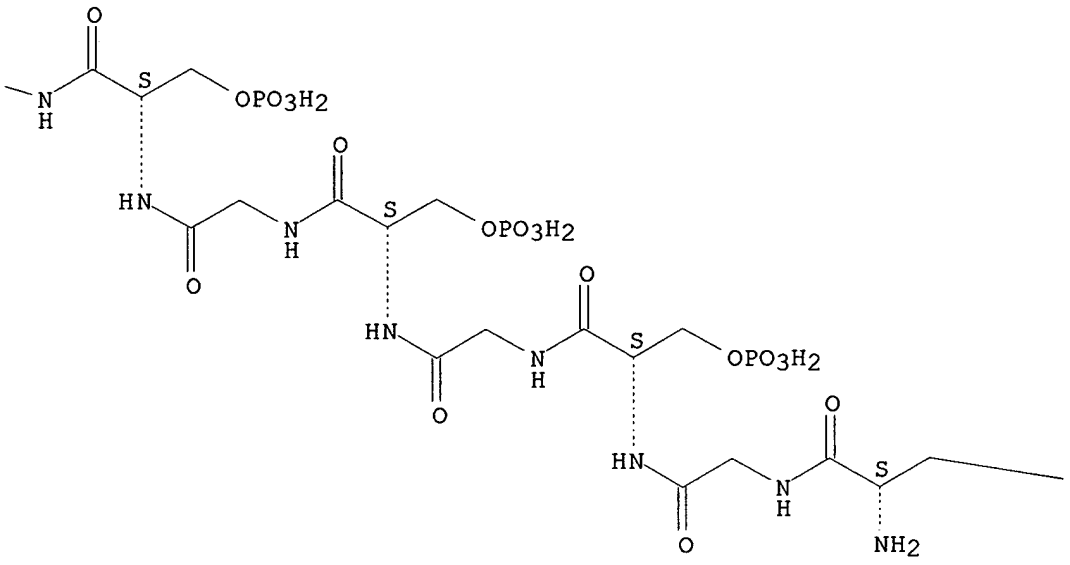


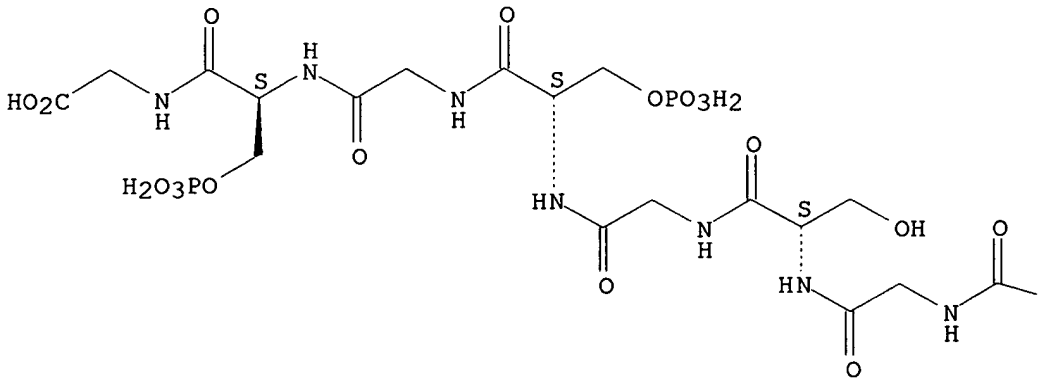
PAGE 1-C

—OPO_3H_2

RN 328896-68-0 HCAPLUS
CN Glycine, L-serylglycyl-L-serylglycyl-L-serylglycyl-L-serylglycyl-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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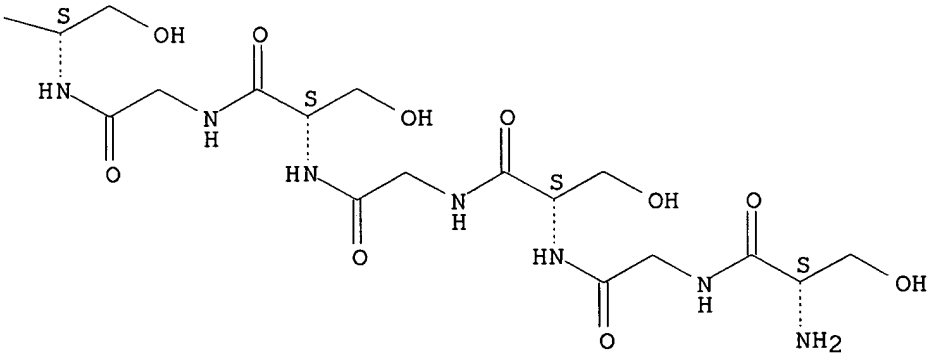
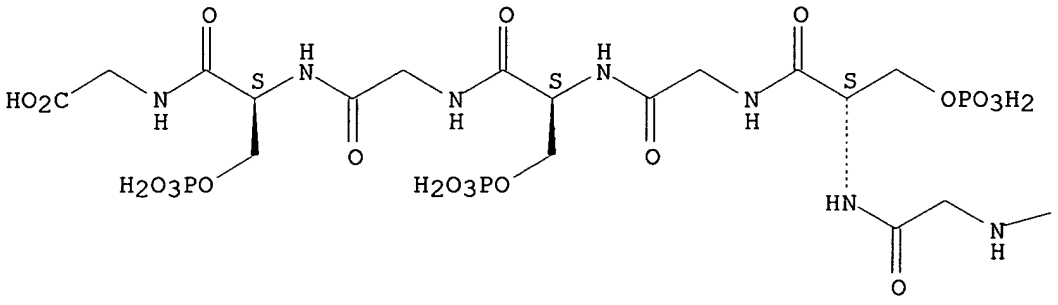


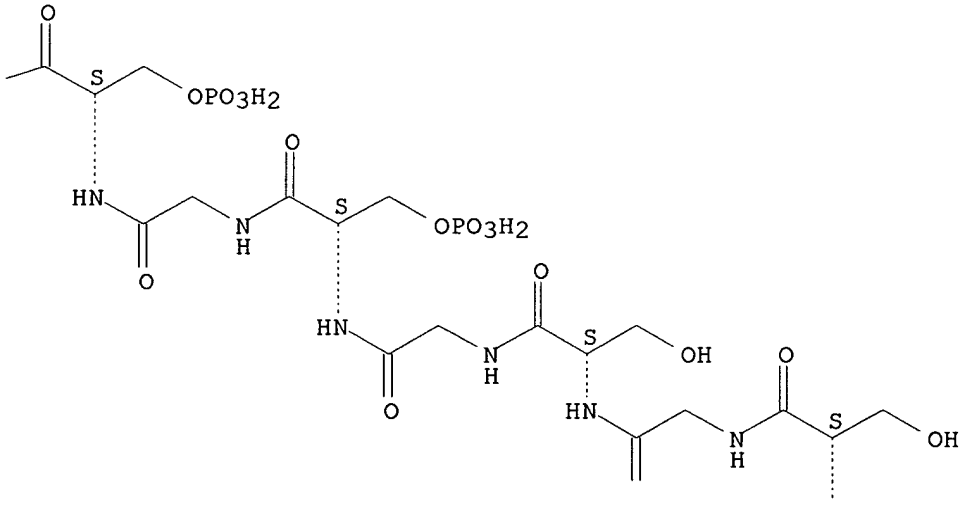
RN 328896-69-1 HCAPLUS
CN Glycine, L-serylglycyl-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-B

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:161806 HCAPLUS
DOCUMENT NUMBER: 128:291691
TITLE: Dentin phosphoprotein sequence motifs and molecular modeling: conformational adaptations to mineral

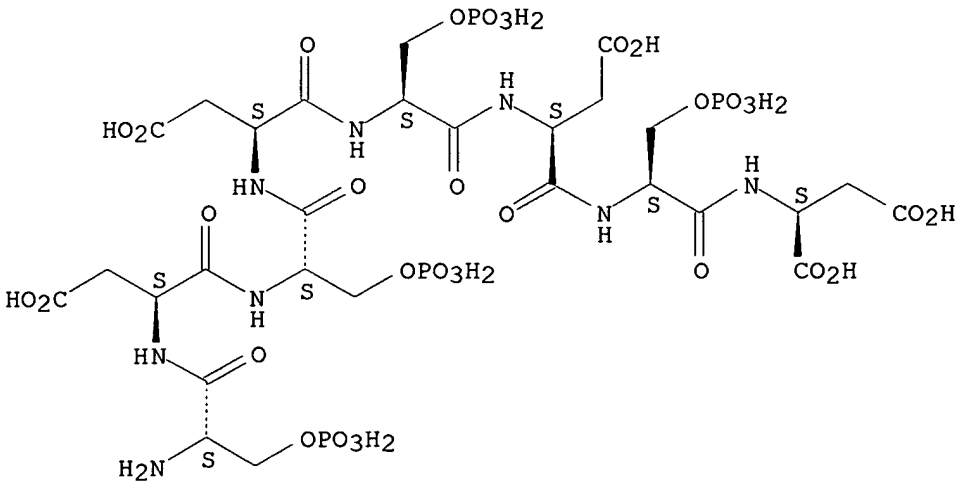
crystals
AUTHOR(S): Dahlin, Stefan; Angstrom, Jonas; Linde, Anders
CORPORATE SOURCE: Dep. Oral Biochem., Goteborg Univ., Goteborg, Swed.
SOURCE: European Journal of Oral Sciences (1998), 106(Suppl. 1), 239-248
CODEN: EJOSFY; ISSN: 0909-8836
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mol. modeling has been used to investigate structural features of oligopeptides derived from possible primary structure motifs in highly phosphorylated dentin phosphoprotein (PP-H), the predominant non-collagenous protein in dentin. It contains a large no. of aspartate (Asp) and phosphoserine (Pse) residues, the latter proposedly crucial for the PP-H function as a mineral nucleator. In this work, computer fitting and subsequent structural adaptation of model peptides, built exclusively from Asp and Pse, to the known crystal structures of hydroxyapatite (HAP) and octacalcium phosphate (OCP) were performed. The results show that, when considering conformational energies of fitted single strand oligo-peptides, either crystal will serve. Within a narrow range, fitting to OCP was slightly better fit to HAP. Energy differences between crystal-adapted and non-adapted freely minimized peptides showed that oligo(Pse-Asp) docked to either HAP or OCP were the energetically most favored adaptations. Fitting of minimized triple anti-parallel .beta.-strands of oligo(Pse-Asp) or oligo (Pse-Pse-Asp), motifs found in published sequences of rat, mouse, and bovine PP-H, revealed that a (001) crystal face of HAP, but most likely not OCP, may be formed by these .beta.-sheet models. The former motif is more advantageous in this respect.

IT **206048-90-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(dentin phosphoprotein sequence motifs and mol. modeling: conformational adaptations to mineral crystals)

RN 206048-90-0 HCAPLUS
CN L-Aspartic acid, O-phosphono-L-seryl-L-.alpha.-aspartyl-O-phosphono-L-seryl-L-.alpha.-aspartyl-O-phosphono-L-seryl-L-.alpha.-aspartyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:55543 HCAPLUS
DOCUMENT NUMBER: 128:110877
TITLE: Synthetic phosphopeptides for treating bone diseases
INVENTOR(S): Kumagai, Yoshinari; Otaka, Akira
PATENT ASSIGNEE(S): Big Bear Bio, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800156	A1	19980108	WO 1997-US11426	19970630
W: AM, AU, BA, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KR, LK, LT, LV, MD, MK, MN, MX, NO, NZ, PL, SG, SI, SK, TR, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5837674	A	19981117	US 1996-675031	19960703
CA 2258661	AA	19980108	CA 1997-2258661	19970630
AU 9735871	A1	19980121	AU 1997-35871	19970630
AU 727675	B2	20001221		
EP 938326	A1	19990901	EP 1997-932409	19970630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2001503452	T2	20010313	JP 1998-504399	19970630

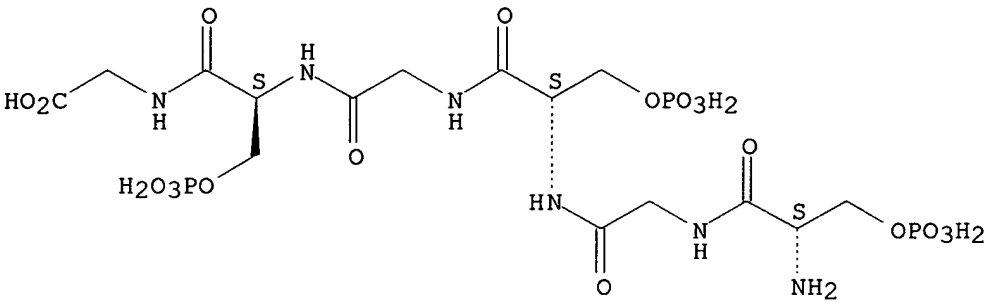
PRIORITY APPLN. INFO.: US 1996-675031 A 19960703
WO 1997-US11426 W 19970630

AB Phosphopeptides which significantly reduce bone loss or weakening are provided. A method for treating or preventing any conditions assocd. with bone loss or weakening by administering the phosphopeptides by oral or injectable means is also provided. After age 35, bone mass, mineral content and mech. strength of the bone begin declining gradually. The relationship between bone mass and age is shown. Examples of prevention of bone loss in an osteoporosis model are given for peptides such as Pse-Gly-Pse-Gly-Pse-Gly (Pse = O-phosphoserine).

IT **201660-41-5 201660-42-6 201660-43-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic phosphopeptides for treating bone diseases)

RN 201660-41-5 HCAPLUS
CN Glycine, O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 201660-42-6 HCAPLUS
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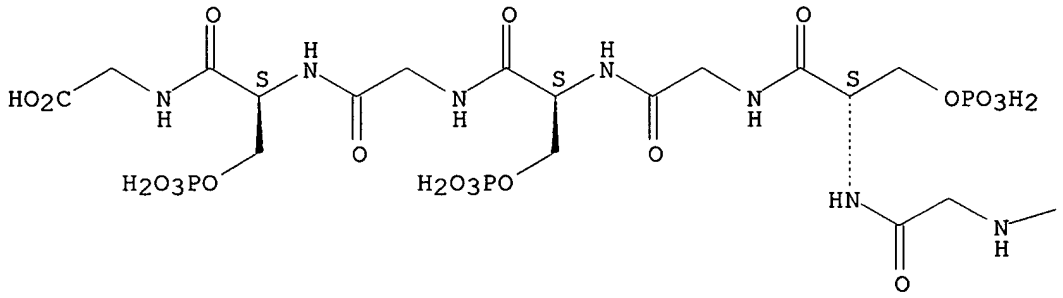
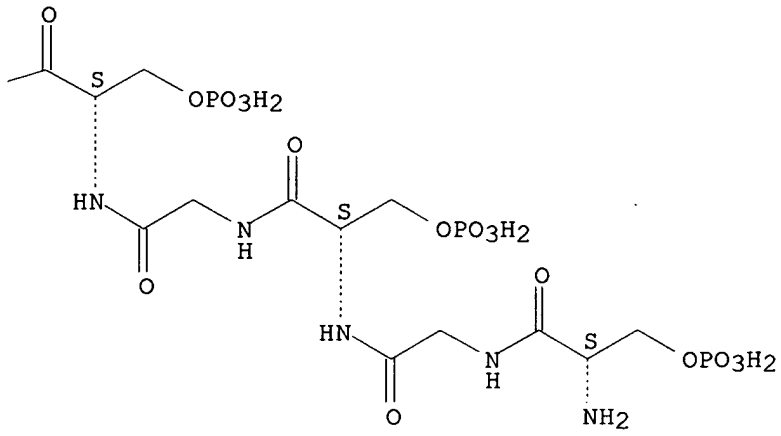
Absolute stereochemistry.

PAGE 1-A



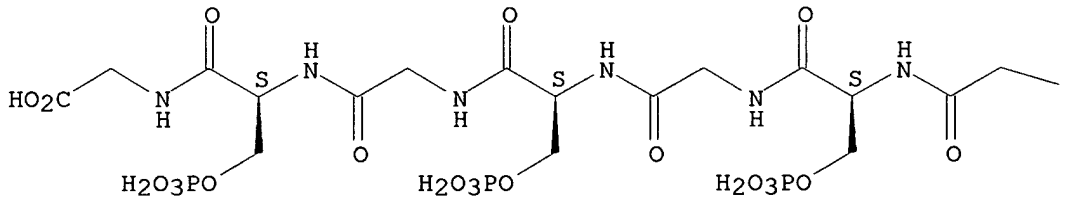
PAGE 1-B



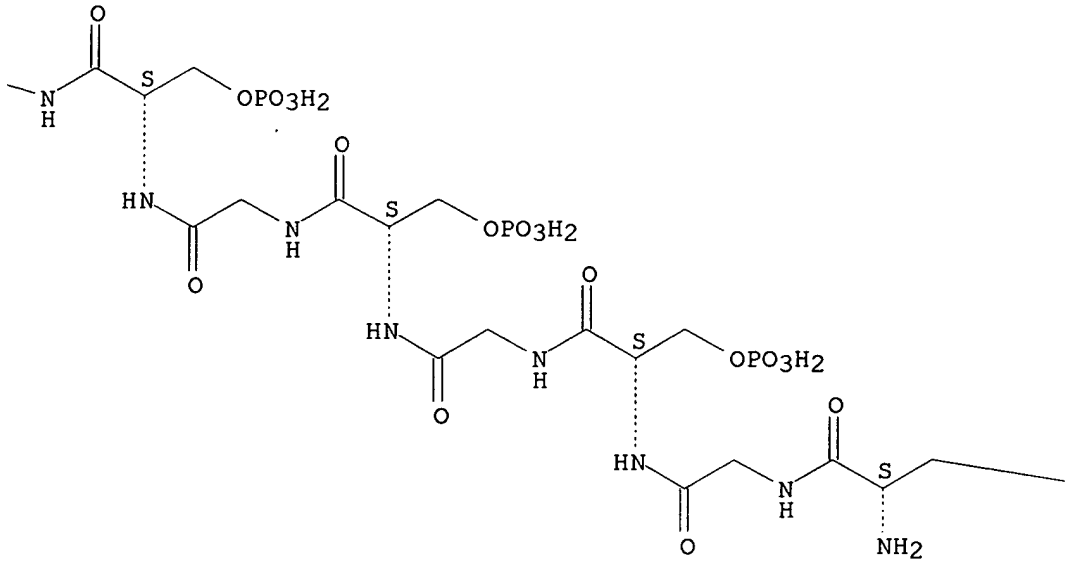
RN 201660-43-7 HCAPLUS
CN Glycine, O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-serylglycyl-O-phosphono-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 1-C

—OPO_3H_2

L19 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:457199 HCAPLUS
DOCUMENT NUMBER: 127:172781
TITLE: High-affinity binding of the Drosophila Numb phosphotyrosine-binding domain to peptides containing a Gly-Pro-(p)Tyr motif
AUTHOR(S): Li, Shun-Cheng; Songyang, Zhou; Vincent, Sebastien J. F.; Zwahlen, Catherine; Wiley, Sandra; Cantley, Lewis; Kay, Lewis E.; Forman-Kay, Julie; Pawson, Tony

CORPORATE SOURCE: Program Molecular Biology Cancer, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, ON, M5G 1X5, Can.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(14), 7204-7209 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The phosphotyrosine-binding (PTB) domain is a recently identified protein module that has been characterized as binding to phosphopeptides contg. an NPXpY motif (X = any amino acid). We describe here a novel peptide sequence recognized by the PTB domain from Drosophila Numb (dNumb), a protein involved in cell fate detn. and asym. cell division during the development of the Drosophila nervous system. Using a Tyr-oriented peptide library to screen for ligands, the dNumb PTB domain was found to bind selectively to peptides contg. a YIGPY.phi. motif (.phi. represents a hydrophobic residue). A synthetic peptide contg. this sequence bound specifically to the isolated dNumb PTB domain in soln. with a dissocn. const. (Kd) of 5.78.+-.0.74 .mu.M. Interestingly, the affinity of this peptide for the dNumb PTB domain was increased (Kd = 1.41.+-.0.10 .mu.M) when the second tyrosine in the sequence was phosphorylated. Amino acid substitution studies of the phosphopeptide demonstrated that a core motif of sequence GP(p)Y is required for high-affinity binding to the dNumb PTB domain. NMR expts. performed on isotopically labeled protein complexed with either Tyr- or pTyr-contg. peptides suggest that the same set of amino acids in the dNumb PTB domain is involved in binding both phosphorylated and nonphosphorylated forms of the peptide. The in vitro selectivity of the dNumb PTB domain is therefore markedly different from those of the Shc and IRS-1 PTB domains, in that it interacts preferentially with a GP(p)Y motif, rather than NPXpY, and does not absolutely require ligand phosphorylation for binding. Our results suggest that the PTB domain is a versatile protein module, capable of exhibiting varied binding specificities.

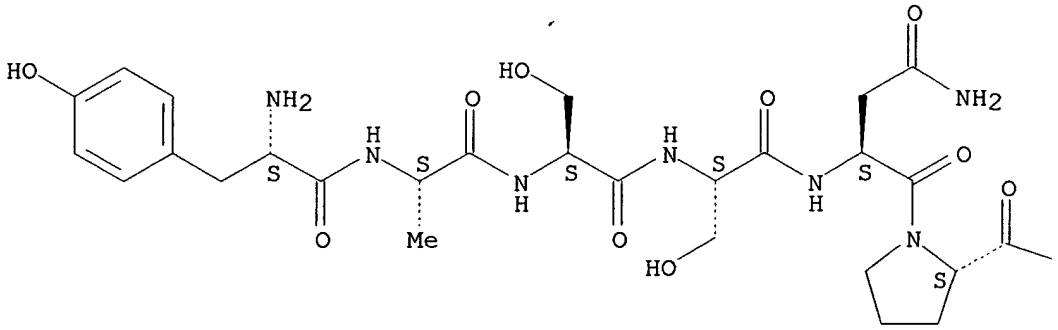
IT **186312-67-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(high-affinity binding of the Drosophila Numb phosphotyrosine-binding domain to peptides contg. a Gly-Pro-(p)Tyr motif)

RN 186312-67-4 HCAPLUS

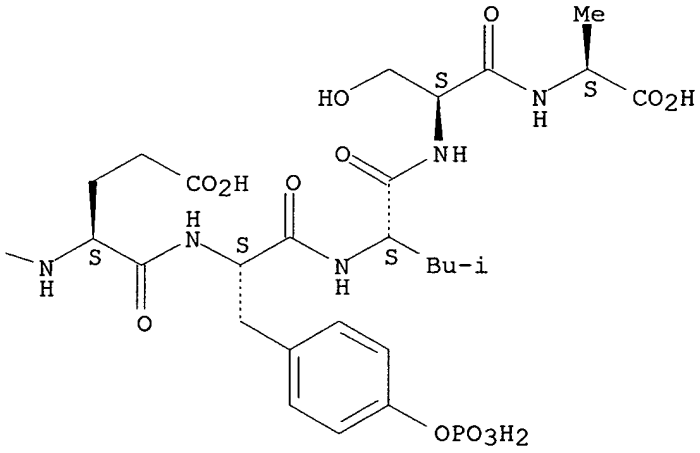
CN L-Alanine, L-tyrosyl-L-alanyl-L-seryl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-glutamyl-O-phosphono-L-tyrosyl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L19 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:377883 HCAPLUS
DOCUMENT NUMBER: 126:338844
TITLE: Phosphotyrosine-containing peptide inhibitors of a phosphotyrosine-binding domain containing protein for the treatment of Shc-dependent conditions
INVENTOR(S): Van Der Geer, Peter; Wiley, Sandra; Gish, Gerald; Pawson, Tony; Toma, Kazunori
PATENT ASSIGNEE(S): Mount Sinai Hospital Corporation, Can.; Asahi Chemical Industry Co., Ltd.; Van Der Geer, Peter; Wiley, Sandra; Gish, Gerald; Pawson, Tony; Toma, Kazunori
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9715318	A1	19970501	WO 1996-US17080	19961024
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ				
CA 2235756	AA	19970501	CA 1996-2235756	19961024
AU 9675211	A1	19970515	AU 1996-75211	19961024
EP 874639	A1	19981104	EP 1996-937741	19961024
R: CH, DE, FR, GB, LI				
JP 11514381	T2	19991207	JP 1996-516793	19961024
US 6028053	A	20000222	US 1998-51934	19980422
PRIORITY APPLN. INFO.:			US 1995-5944P P	19951027
			US 1996-10384P P	19960122
			US 1996-11799P P	19960220
			WO 1996-US17080 W	19961024

AB Phosphotyrosine-contg. peptides derived from the Asn-Pro-X-phosphoTyr motif found in phosphotyrosine-contg. proteins are described. These peptides interfere with the binding of proteins to the phosphotyrosine-binding domains and can be used to control signal transduction processes, esp. those involving SH domain-contg. proteins. The peptides may be prepd. by std. chem. or biol. by expression of the corresponding gene or incorporation into a fusion protein.

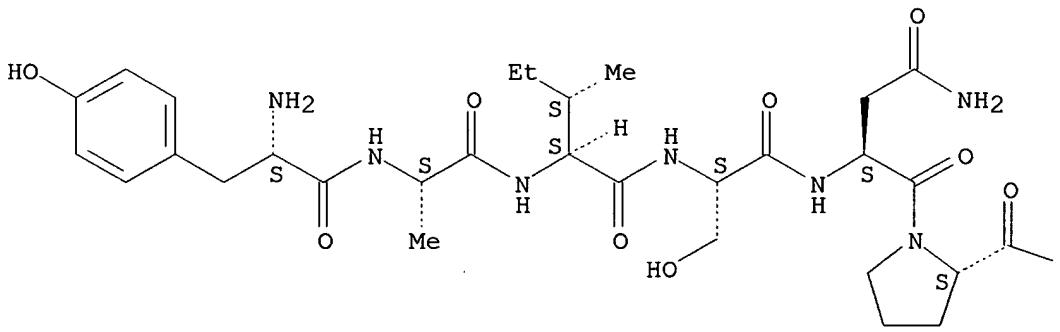
IT **186312-68-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence, inhibition of Shc binding to growth factor receptors and; phosphotyrosine-contg. peptide inhibitors of phosphotyrosine-binding domain contg. protein for treatment of Shc-dependent conditions)

RN 186312-68-5 HCAPLUS

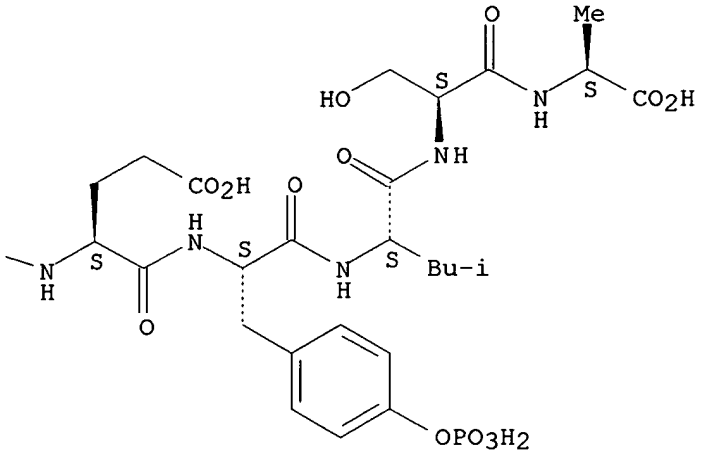
CN L-Alanine, L-tyrosyl-L-alanyl-L-isoleucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-glutamyl-O-phosphono-L-tyrosyl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L19 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:21554 HCAPLUS
DOCUMENT NUMBER: 126:114763
TITLE: Characterization of the phosphotyrosine-binding domain of the Drosophila Shc protein
AUTHOR(S): Li, Shun-Cheng; Lai, Ka-Man Venus; Gish, Gerald D.; Parris, Wendy E.; van der Geer, Peter; Forman-Kay, Julie; Pawson, Tony
CORPORATE SOURCE: Samuel Lunenfeld Res. Inst., Mt. Sinai Hosp., Toronto, ON, M5G 1X5, Can.
SOURCE: Journal of Biological Chemistry (1996), 271(50), 31855-31862
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The phosphotyrosine-binding (PTB) domain of Drosophila Shc (dShc) binds in vitro to phosphopeptides contg. the sequence motif NPXpY, and phys. assocs. with the activated Drosophila epidermal growth factor receptor homolog (DER) in vivo. The structural elements, specificity and binding kinetics of the dShc PTB domain have now been characterized. The dShc PTB domain appeared similar to the insulin-like receptor substrate-1 PTB domain in secondary structure as suggested by Fourier transform IR spectroscopy. Surface plasmon resonance measurements indicated that the dShc PTB domain bound with high affinity to phosphopeptides (Der) derived from the Tyr1228 site of the DER receptor. The kinetics of the dShc PTB domain-Der phosphopeptide interaction differed from those of a typical SH2 domain-ligand interaction, in that the PTB domain displayed slower on/off rates. Competition binding assays using truncated versions of the Der peptides revealed that high affinity binding to the dShc PTB domain requires, in addn. to the NPXpY motif, the presence of hydrophobic residues at both positions -5 and -7 relative to phosphotyrosine. The dShc PTB domain showed a similar binding specificity to the human Shc (hShc) PTB domain, but subtle differences were noted; such that the hShc

PTB domain bound preferentially to a phosphopeptide from the mammalian nerve growth factor receptor, whereas the dShc PTB domain bound preferentially to phosphopeptides from the Drosophila DER receptor. The invertebrate dShc PTB domain therefore possesses a binding specificity for tyrosine-phosphorylated peptides that is optimally suited for recognition of the activated DER receptor.

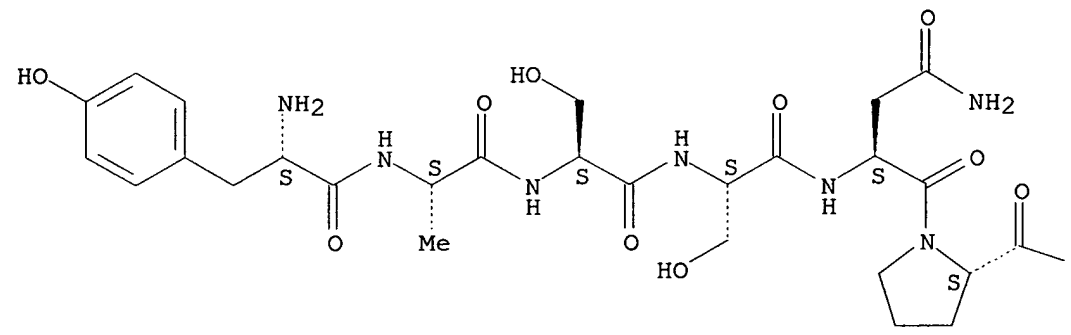
IT **186312-67-4 186312-68-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(characterization of phosphotyrosine-binding domain of Shc protein)

RN 186312-67-4 HCAPLUS

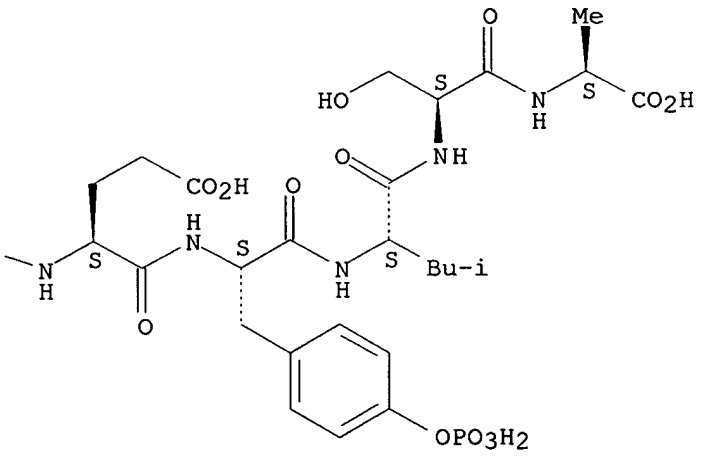
CN L-Alanine, L-tyrosyl-L-alanyl-L-seryl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-glutamyl-O-phosphono-L-tyrosyl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



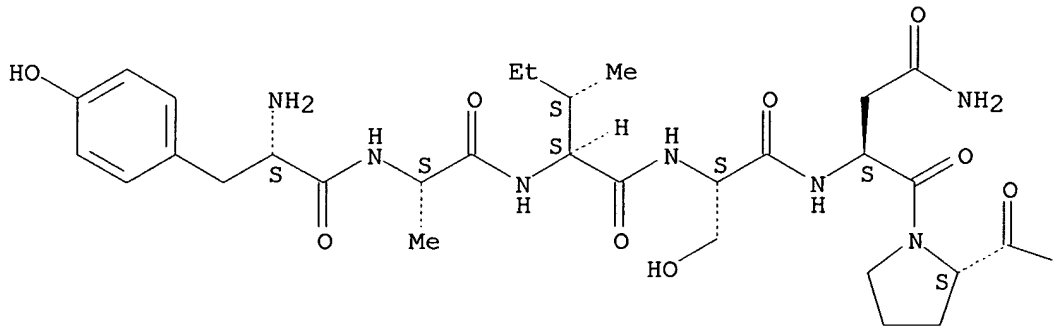
RN 186312-68-5 HCAPLUS

CN L-Alanine, L-tyrosyl-L-alanyl-L-isoleucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-glutamyl-O-phosphono-L-tyrosyl-L-leucyl-L-seryl- (9CI) (CA INDEX

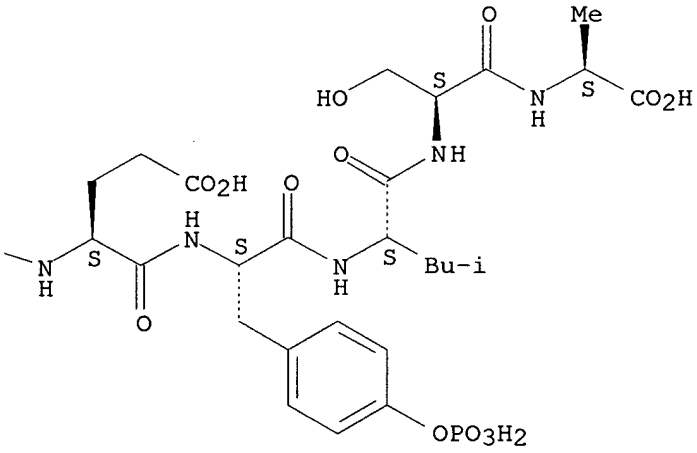
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L19 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:153236 HCAPLUS
DOCUMENT NUMBER: 124:220717
TITLE: Systematic mapping of potential binding sites for Shc and Grb2 SH2 domains on insulin receptor substrate-1 and the receptors for insulin, epidermal growth factor, platelet-derived growth factor, and fibroblast growth factor
AUTHOR(S): Ward, Colin W.; Gough, Keith H.; Rashke, Melisa; Wan, Soo San; Tribbick, Gordon; Wang, Jian-xin
CORPORATE SOURCE: Division Biomolecular Engineering, CSIRO, Parkville, 3052, Australia
SOURCE: Journal of Biological Chemistry (1996), 271(10), 5603-9
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Multipin peptide synthesis has been employed to produce biotinylated 11-mer phosphopeptides that account for every tyrosine residue in insulin receptor substrate-1 (IRS-1) and the cytoplasmic domains of the insulin-, epidermal growth factor-, platelet-derived growth factor- and basic fibroblast growth factor receptors. These phosphopeptides have been screened for their capacity to bind to the SH2 domains of Shc and Grb in a soln. phase ELISA. The data revealed new potential Grb2 binding sites at Tyr-1114 (epidermal growth factor receptor (EGFR) C-tail); Tyr-743 (platelet-derived growth factor receptor (PDGFR) insert region), Tyr-1110 from the E-helix of the catalytic domain of insulin receptor (IR), and Tyr-47, Tyr-939, and Tyr-727 in IRS-1. None of the phosphopeptides from the juxtamembrane or C-tail regions of IR bound Grb2 significantly, and only one phosphopeptide from the basic fibroblast growth factor receptor (Tyr-556) bound Grb2 but with medium strength. Tyr-1068 and -1086 from the C-tail of EGFR, Tyr-684 from the kinase insert region of PDGFR, and Tyr-895 from IRS-1 were confirmed as major binding sites for the Grb2 SH2 domain. With regard to Shc binding, the data revealed new potential binding sites at Tyr-703 and Tyr-789 from the catalytic domain of EGFR and at Tyr-557 in the juxtamembrane region of PDGFR. It also identified new potential Shc binding sites at Tyr-764, in the C-tail of basic fibroblast growth factor receptor, and Tyr-960, in the juxtamembrane of IR, a residue previously known to be required for Shc phosphorylation in response to insulin. The study confirmed the previous identification of Tyr-992 and Tyr-1173 in the C-tail of EGFR and several phosphopeptides from the PDGFR as medium strength binding sites for the SH2 domain of Shc. None of the 34 phosphopeptides from IRS-1 bound Shc strongly, although Tyr-690 showed medium strength binding. The specificity characteristics of the SH2 domains of Grb2 and Shc are discussed. This systematic peptide mapping strategy provides a way of rapidly scanning candidate proteins for potential SH2 binding sites as a first step to establishing their involvement in kinase-mediated signaling pathways.

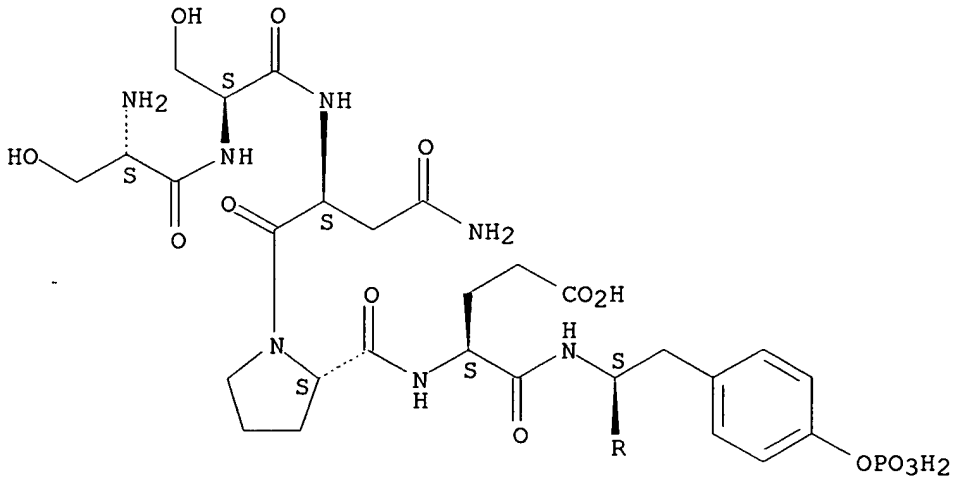
IT **174660-15-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(Shc and Grb2 SH2 domain binding site mapping on insulin receptor substrate-1 and insulin receptor and growth factor receptors)

RN 174660-15-2 HCAPLUS

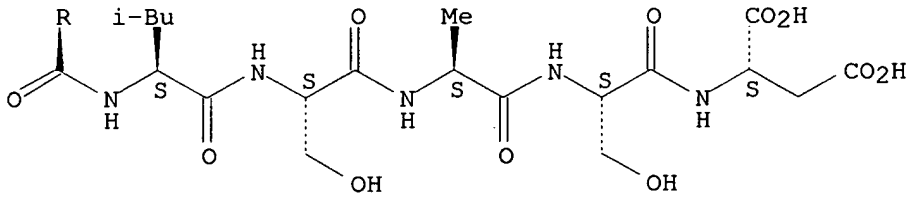
CN L-Aspartic acid, N-[N-[N-[N-[N-[O-phosphono-N-[N-[1-[N2-(N-L-seryl-L-seryl)-L-asparaginyl]-L-prolyl]-L-.alpha.-glutamyl]-L-tyrosyl]-L-leucyl]-L-seryl]-L-alanyl]-L-seryl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L19 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:541384 HCAPLUS
DOCUMENT NUMBER: 122:282231
TITLE: Peptide inhibitors of mitogenesis and motogenesis
INVENTOR(S): Comoglio, Paolo; Ponzetto, Carola
PATENT ASSIGNEE(S): Farmitalia Carlo Erba S.r.L., Italy
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9501376	A1	19950112	WO 1994-EP1943	19940615
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2142713	AA	19950112	CA 1994-2142713	19940615
AU 9470718	A1	19950124	AU 1994-70718	19940615
AU 670704	B2	19960725		
EP 662090	A1	19950712	EP 1994-919632	19940615

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE

CN 1111455	A	19951108	CN 1994-190440	19940615	
CN 1056153	B	20000906			
HU 71324	A2	19951128	HU 1995-919	19940615	
HU 219813	B	20010828			
JP 08500845	T2	19960130	JP 1994-521434	19940615	
RU 2146262	C1	20000310	RU 1995-108385	19940615	
PL 179628	B1	20001031	PL 1994-307742	19940615	
US 5594105	A	19970114	US 1994-266514	19940627	
ZA 9404680	A	19950215	ZA 1994-4680	19940629	
IL 110160	A1	20000629	IL 1994-110160	19940629	
FI 9500729	A	19950419	FI 1995-729	19950217	
US 5912183	A	19990615	US 1996-654604	19960529	

PRIORITY APPLN. INFO.:

GB 1993-13528	A	19930630
GB 1994-7673	A	19940418
WO 1994-EP1943	W	19940615
US 1994-266514	A3	19940627

AB Novel peptides having the sequence of a portion of Shc protein, which peptide can bind to intracellular signal transducers and thus interfere with signal transduction pathways leading to cell proliferation and motility, are provided. The peptides of the invention may be chem. synthesized from single amino acids and/or peptides of two or more amino acid residues. The peptides of the invention find a useful application in the treatment of a neoplastic disease.

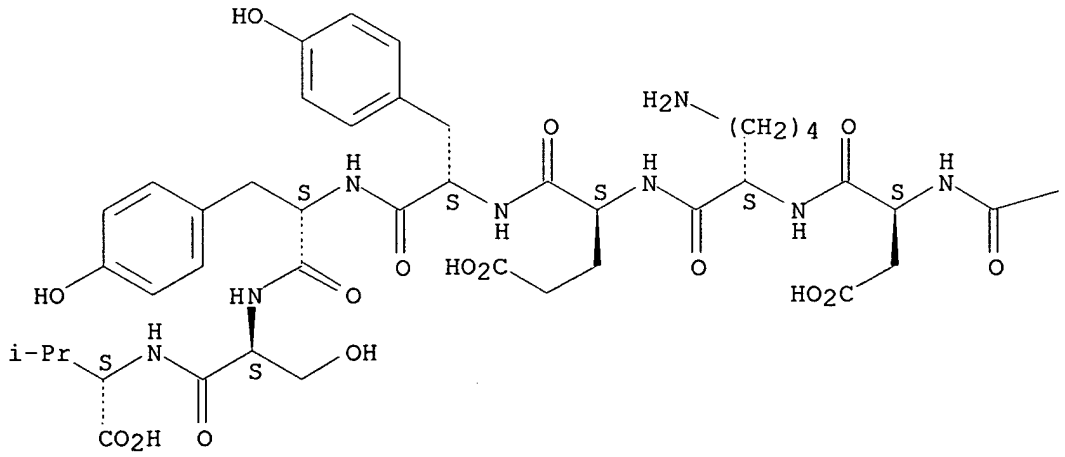
IT **162923-98-0P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oligopeptide contg. Shc protein fragment for interfering intracellular signal transduction and use as inhibitors of mitogenesis and motogenesis)

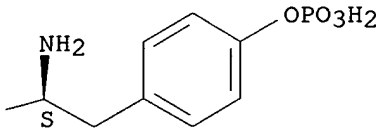
RN 162923-98-0 HCAPLUS

CN L-Valine, N-[N-[N-[N-[N-[N2-[N-(O-phosphono-L-tyrosyl)-L-.alpha.-aspartyl]-L-lysyl]-L-.alpha.-glutamyl]-L-tyrosyl]-L-tyrosyl]-L-seryl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



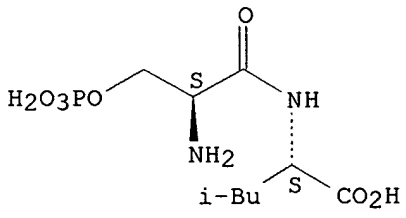


L19 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:492927 HCAPLUS
DOCUMENT NUMBER: 115:92927
TITLE: Synthesis of casein-related peptides and phosphopeptides. XIV. Solid-phase synthesis of Glu-Ser(P)-Leu through the use of protected Boc-Ser(PO3R2)-OH derivatives
AUTHOR(S): Perich, John W.; Valerio, Robert M.; Alewood, Paul F.; Johns, R. B.
CORPORATE SOURCE: Sch. Chem., Univ. Melbourne, Parkville, 3052, Australia
SOURCE: Australian Journal of Chemistry (1991), 44(6), 771-8
CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A solid-phase method is described for the synthesis of O-phosphoseryl-contg. peptides H-Glu-Ser(PO3R2)-Leu-OH (I; R = H, Et) and H-Ser(PO3H2)-Leu-OH with Boc-Ser(PO3R2)-OH (Boc = Me3CO2C; R = Et, Ph, CMe3) and PhCMe2O2-Ser[PO3(CH2Ph)2]-OH for the incorporation of the phosphorylated seryl residue.

IT **135432-35-8P 135432-36-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 135432-35-8 HCAPLUS
CN L-Leucine, N-(O-phosphono-L-seryl)-, monohydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



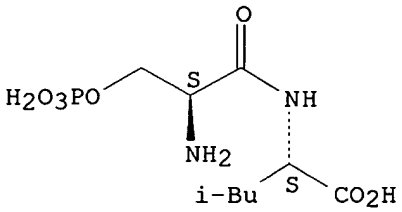
HBr

RN 135432-36-9 HCAPLUS
CN L-Leucine, N-(O-phosphono-L-seryl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

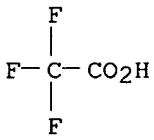
CRN 6665-27-6
CMF C9 H19 N2 O7 P

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

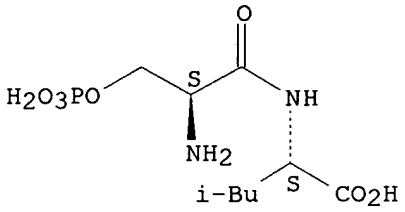


L19 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:186053 HCAPLUS
DOCUMENT NUMBER: 114:186053
TITLE: Synthesis of casein-related peptides and phosphopeptides. VIII. The synthesis of Ser(P)-containing peptides by the use of Z-Ser(PO3R2)-OH derivatives
AUTHOR(S): Perich, John W.; Alewood, Paul F.; Johns, R. B.
CORPORATE SOURCE: Sch. Chem., Univ. Melbourne, Parkville, 3052, Australia
SOURCE: Australian Journal of Chemistry (1991), 44(2), 253-63
CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:186053
AB The synthesis of five Z-Ser(PO3R2)-OH (I; Z = PhCH2O2C; R = Ph, Et, Me, CH2Ph, CMe3) is described by a simple three-step synthetic procedure which features the use of either di-Ph or dialkyl phosphorochloridate/pyridine or dialkyl N,N-diethylphosphoramidite/1H-tetrazole-m-chloroperoxybenzoic acid for the phosphorylation of the serine hydroxy group. The benzyl phosphate deriv. I (R = CH2Ph) was used in the benzyloxycarbonyl mode of peptide synthesis for the prepn. of Z-Ser[PO3(CH2Ph)2]-X-OCH2Ph [X = Leu,

Ser[PO3(CH2Ph)2]] which were deprotected by palladium-catalyzed hydrogenolysis to give the corresponding phosphoserine dipeptides in high yields and high purity.

IT **6665-27-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 6665-27-6 HCAPLUS
CN L-Leucine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



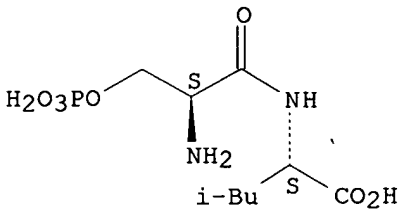
L19 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:186052 HCAPLUS
DOCUMENT NUMBER: 114:186052
TITLE: Synthesis of casein-related peptides and phosphopeptides. VII. The efficient synthesis of Ser(P)-Containing peptides by the use of Boc-Ser(PO3R2)-OH derivatives
AUTHOR(S): Perich, John W.; Alewood, Paul F.; Johns, R. B.
CORPORATE SOURCE: Sch. Chem., Univ. Melbourne, Parkville, 3052, Australia
SOURCE: Australian Journal of Chemistry (1991), 44(2), 233-52
CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:186052

AB A new approach to the synthesis of Ser(PO3R2)-contg. peptides by using five protected Boc-Ser(PO3R2)-OH (I; Boc = Me3CO2C; R = Ph, Et, Me, CH2Ph, CMe3) derivs. is described. I are prepd. by a simple three-step synthetic procedure which features the use of either di-Ph or dialkyl phosphorochloridate/pyridine, or dialkyl N,N-diethylphosphoramidite/1H-tetrazole-m-chloroperoxybenzoic acid for the phosphorylation of the serine hydroxy group. I were utilized in the Boc mode of peptide synthesis with the use of the mixed anhydride coupling procedure, and led to the synthesis of the protected tripeptides, Boc-Glu(OCH2Ph)-Ser(PO3R2)-Leu-OCH2Ph in high yield and purity. In peptide deprotection studies, the Ph and benzyl phosphate protecting groups were readily removed from the protected tripeptides by hydrogenolysis and gave the phosphoserine tripeptide in near quant. yield. The tert-Bu phosphate groups were cleaved from Boc-Ser[PO3(CMe3)2]-Leu-OCH2Ph by mild acidolysis and gave the phosphoserine dipeptide in quant. yield. However, attempts to cleave the Et or Me phosphate groups by acidolytic or silylitic treatment of the corresponding tripeptides resulted in decompn. of the O-phosphoseryl residue.

IT **6665-27-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

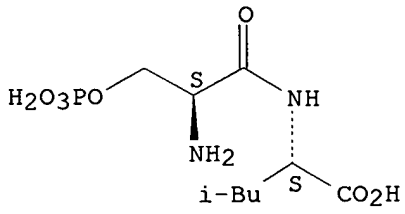
RN 6665-27-6 HCAPLUS
CN L-Leucine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:176857 HCAPLUS
DOCUMENT NUMBER: 106:176857
TITLE: Fast-atom-bombardment mass spectrometry of seryl- and O-phosphoseryl-containing peptides
AUTHOR(S): Johns, R. B.; Alewood, P. F.; Perich, J. W.; Chaffee, A. L.; MacLeod, J. K.
CORPORATE SOURCE: Dep. Org. Chem., Univ. Melbourne, Parkville, 3052, Australia
SOURCE: Tetrahedron Letters (1986), 27(39), 4791-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
AB O-Phosphoserine (PSer) and peptides PSer-Leu and Glu-PSer-Leu were analyzed by fast-atom-bombardment mass spectrometry (FAB-MS). FAB-MS can be used for mol. wt. detn., sequence elucidation, and characterization of PSer-contg. peptides. A loss of 98 mass units is a diagnostic test for the identification of a PSer residue in a peptide.
IT **6665-27-6**
RL: PRP (Properties)
(fast-atom-bombardment mass spectrum of)
RN 6665-27-6 HCAPLUS
CN L-Leucine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

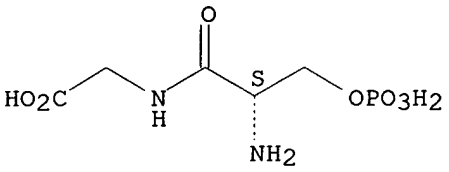
Absolute stereochemistry.



L19 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:85018 HCAPLUS
DOCUMENT NUMBER: 106:85018
TITLE: Solid-phase synthesis of phosphopeptides: synthesis of phosphopeptides from the carboxyl-terminus of rhodopsin

AUTHOR(S): Arendt, Anatol; Hargrave, Paul A.
CORPORATE SOURCE: Dep. Ophthalmol., Univ. Florida, Gainesville, FL, 32610, USA
SOURCE: Pept.: Struct. Funct., Proc. Am. Pept. Symp., 9th (1985), 237-40
CODEN: 54ZNAJ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Me3CO2CNHCH(CO2H)CHROP(O)(OPh)2 (R = H, Me) were prepd. and used in the solid-phase synthesis of phosphorylated serine (PSer) and threonine (PThr) contg. peptides H-PSer-Gly-OH, H-Val-PSer-Lys-OH, H-Glu-PThr-PSer-Gln-Val-OH, and H-Val-Ser-Lys-Thr-Glu-PThr-PSer-Gln-Val-OH.
IT **6665-42-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 6665-42-5 HCAPLUS
CN Glycine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:2581 HCAPLUS
DOCUMENT NUMBER: 100:2581
TITLE: Tripeptidyl aminopeptidase in the extralysosomal fraction of rat liver
AUTHOR(S): Baaloew, Ros Mari; Ragnarsson, Ulf; Zetterqvist, Oerjan
CORPORATE SOURCE: Biomed. Cent., Univ. Uppsala, Uppsala, S-751 23, Swed.
SOURCE: Journal of Biological Chemistry (1983), 258(19), 11622-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tripeptidyl aminopeptidase (I), an enzyme which removes tripeptides from the free, N-terminal end of oligopeptides, was detected in the extralysosomal fraction of rat liver. I was partially purified by Sepharose CL-4B and DEAE-cellulose chromatog. The pH optimum was in the neutral range and the apparent native mol. wt. was >106, as judged by Sepharose chromatog. I cleaved the phosphopeptide, Gly-Val-Leu-Arg-Arg-Ala-Ser(P)-Val-Ala, 1st at the Leu-Arg bond and then at the Ala-Ser(P) bond. The cleavage of the former bond was inhibited by Arg-Arg-Ala-Ser(P)-Val-Ala (II), which indicated that both bonds were cleaved by the same enzyme. The Km for II was 0.01 mM at pH 6.5-7.5. Val-Leu-Arg-Arg-Ala-Ser(P)-Val-Ala (III) and Leu-Arg-Arg-Ala-Ser(P)-Val-Ala were poor substrates. III was, however, an efficient inhibitor. The Ala-Ser(P) bond of Arg-Arg-Ala-Ser(P)-Val (IV) was cleaved at the same rate as that of II. I was active also with the unphosphorylated peptides corresponding to II and IV and tolerated the substitution of lysine for

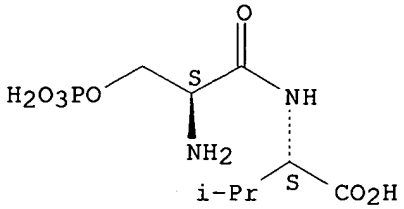
the N-terminal arginine of the latter peptide. Substitution of guanidovaleric acid for the N-terminal arginine of IV and of guanidovaleric acid or .epsilon.-aminohexanoic acid for the N-terminal arginine of unphosphorylated IV reduced the rate of hydrolysis to insignificant levels, demonstrating the importance of a free N-terminus. The results thus provide evidence of a unique I.

IT **88169-78-2**
RL: FORM (Formation, nonpreparative)
(formation of, by tripeptidyl aminopeptidase of liver)

RN 88169-78-2 HCAPLUS

CN L-Valine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1971:482043 HCAPLUS

DOCUMENT NUMBER: 75:82043

TITLE: Ultraviolet, visible, and infrared spectroscopic studies of the interaction of hydroxocobalamin with .alpha.-amino acids and peptides

AUTHOR(S): Heathcote, J. G.; Moxon, G. H.; Slifkin, M. A.

CORPORATE SOURCE: Univ. Salford, Salford, Engl.

SOURCE: Spectrochim. Acta, Part A (1971), 27(8), 1391-408
CODEN: SAMCAS

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Evidence is given for the formation of mol. complexes between vitamin B12b and certain .alpha.-amino acids, with a mol. ratio of 1.1. Infrared data show that charge donation occurs from the N of the amino acid, in the unionized form. Rate consts. for complex formation are also given. Evidence is presented for the formation of mol. complexes between hydroxocobalamin (vitamin B12b) and dipeptides, polypeptides, or proteins. It is obsd. that hydroxocobalamin forms a complex with glycine more readily than with other .alpha.-amino acids. This extends to peptides also; thus, peptides contg. N-terminal glycine complex more strongly than those contg. other N-terminal amino acids. Nevertheless, other amino acids, in particular the 2nd amino acid in the chain, play a part in detg. complexing ability. There is a significant decrease in assocn. as one goes down the series Ala-Gly, Ala-Ala, Ala-Ser. Steric effects also appear to be important.

IT **33897-83-5**
RL: PRP (Properties)
(spectrum of)

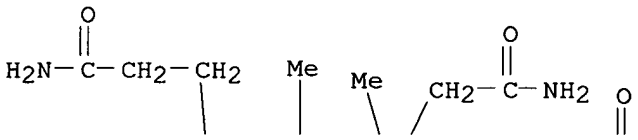
RN 33897-83-5 HCAPLUS

CN Cobinamide, dihydroxide, dihydrogen phosphate (ester), mono(inner salt), 3'-ester with 5,6-dimethyl-1-.alpha.-D-ribofuranosylbenzimidazole, compd. with N-L-serylglycine (1:1) (8CI) (CA INDEX NAME)

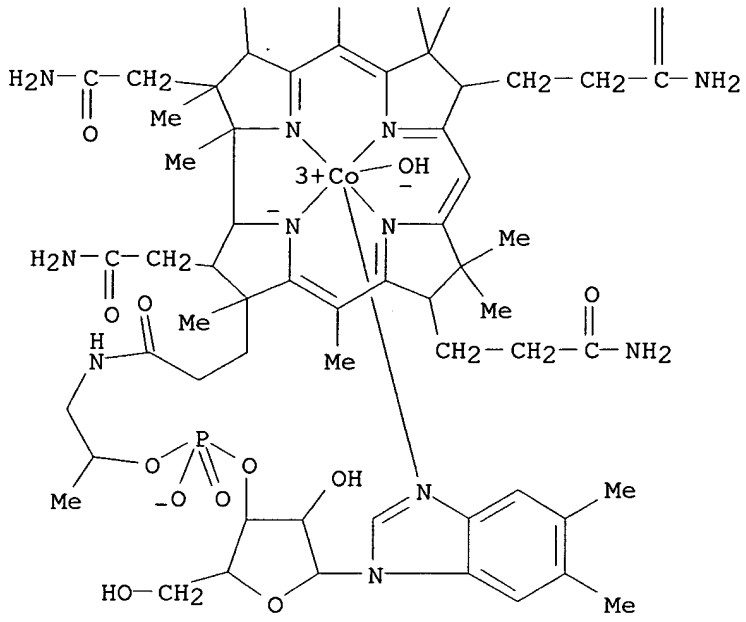
CM 1

CRN 13422-51-0
CMF C62 H89 Co N13 O15 P
CCI CCS

PAGE 1-A



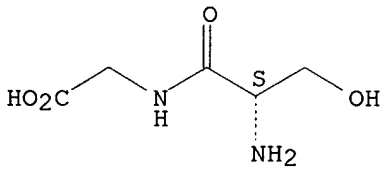
PAGE 2-A



CM 2

CRN 687-63-8
CMF C5 H10 N2 O4

Absolute stereochemistry.



L19 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1966:412631 HCAPLUS
DOCUMENT NUMBER: 65:12631
ORIGINAL REFERENCE NO.: 65:2346f-h,2347a-h,2348a-h,2349a-e
TITLE: Synthesis of phosphopeptides. V. Further dipeptides, tripeptides, and O-phosphorylated derivatives of L-serine
AUTHOR(S): Folsch, Georg
CORPORATE SOURCE: Univ. Goteborg, Swed.
SOURCE: Acta Chem. Scand. (1966), 20(2), 459-73
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. CA 57, 4794h. Various phosphorylated di- and tripeptides as well as the corresponding phosphate-free peptides were synthesized via N-benzyloxycarbonyl peptide benzyl esters. Protected di- and tripeptide derivs. of .beta.-Bzl-Asp-Set (Bzl = benzyl) all underwent a rapid

cyclization to aspartimides under weakly alk. conditions, e.g. when dissolved in C5H5N-H2O, whereas the corresponding derivs. of .gamma.-Bzl-Glu-Ser were stable under the same conditions. Some further new derivs. of serine and threonine were prepd. and studied. (All amino acids used have the L-configuration, except glycine. Z = PhCH2O2C; SerP = phosphorylserine = H2NCH(CH2OPO3H2)-CO2H; DCCI = dicyclohexylcarbodiimide; THF = tetrahydrofuran). Z-Aspartic acid .beta.-Bzl ester (Ia) (Benoiton, CA 57, 9943g) (3.6 g.), 3.6 g. serine Bzl ester benzenesulfonate (I) (CA 56, 7418e), 1.4 ml. Et3N, and 2.1 g. DCCI in 100 ml. 1:1 THF-MeCN shaken 4 hrs. at 4.degree. and 18 hrs. at room temp. and the soln. filtered, concd. in vacuo at 40.degree., and poured into 1 l. ice H2O with stirring gave 4.4 g. Z-.alpha.-Asp-Ser-(Bzl)2 (II), m. 129.degree. (EtOAc-Et2O), [.alpha.]26D 6.9.degree. (c 5.8, AcOH), [.alpha.]26D 0.degree. (c 3.0, C5H5N). The optical rotation of II (300 mg.) increased steadily when dissolved in 10.5 ml. C5H5N and 4.5 ml. H2O. After 5 days at 26.degree., the soln. was evapd. in vacuo and the residue triturated with Et2O to give 120 mg. solid, m. 118-22.degree., which was hydrogenolyzed in tert-BuOH-H2O. Paper chromatographic analysis of the product formed showed the presence of 3 ninhydrin-pos. compds. One of the spots gave the normal purple color and had the Rf 0.50 [2:1:1:1 BuOH-MeOH-HCO2H-H2O (solvent A)] of .alpha.-Asp-Ser (IIa). A brownish spot of about the same intensity [Rf 0.59 (A)], apparently representing the main product, gave a bright yellow color and corresponded to the aspartimide .alpha.,.beta.-Asp-Ser. The ir spectrum of the mixt. differed from that of IIa mainly in the carbonyl region. The absorption band was now split into well-sepd. peaks at 5.80 and 6.1 .mu., as in the case of succinimide. .alpha.-Bzl Z-glutamate (3.7 g.), 3.6 g. I, 1.4 ml. Et3N, and 2.1 g. DCCI in 50 ml. 1:1 THF-MeCN treated like II, the soln. filtered and evapd. in vacuo, the residue dissolved in CH2Cl2, and the soln. filtered, washed successively with M HCl, H2O, satd. aq. NaHCO3, and H2O, dried, and evapd. gave 4.1 g. Z-.gamma.-Glu-Ser-(Bzl)2, m. 118.degree. (EtOAc-Et2O), [.alpha.]27D 1.2.degree. (c 4.0, AcOH). From 8.0 g. oily Z-isoleucine was prepd. as above 9.8 g. Z-Ile-Ser-Bzl, m. 175.degree. (EtOAc), [.alpha.]25D -17.9.degree. (c 6.1, AcOH). From 8.3 g. N.alpha., N.epsilon.Z2-lysine was prepd. as above 9.4 g. N.alpha.,N.epsilon.-Z2-Lys-Ser-Bzl (III); when crystd. from EtOAc-ligroine, III m. 144.degree.; when crystd. from EtOAc-Et2O, III frequently m. 122.degree., solidified, and then m. 144.degree.; the optical rotations of the 2 forms were identical, [.alpha.]26D -4.8.degree. (c 6.1, AcOH), indicating dimorphism. From Z-glycine was prepd. as above Z-Gly-Ser-Bzl IIIc, m. 149.degree. (EtOAc), 4.7.degree. (c 6.1, AcOH). From 4.8 g. Z-serine and 7.0 g. alanine Bzl ester p-toluenesulfonate (IV) was prepd. 12.7 g. Z-Ser-Ala-Bzl, m. 117.degree. (EtOAc-Et2O), [.alpha.]26 D -22.1.degree. (c 5.9, AcOH). The mixed anhydride, prepd. at -5.degree. from 3.7 g. .gamma.-Bzl Z-glutamate (V), 1.4 ml. Et3N, and 0.95 ml. ClCO2Et in 40 ml. dry 1:1 dioxane-THF, was kept 15 min. at -5.degree., a cold (-5.degree.) soln. of 2.1 g. serine in 5.0 ml. 4M NaOH added, the mixt. shaken 30 min. at room temp., the org. solvents removed in vacuo, the residual alk. soln. acidified with 3M HCl, and the product isolated with Et2O to give 2.4 g. Z-.alpha.-Glu-Ser-.gamma.-Bzl, m. 62-4.degree. (EtOAc-ligroine); 88% dicyclohexylammonium salt (VI) m. 180.degree.. Free dipeptides (10 millimoles), 10 ml. PhCH2OH, 11 millimoles p-MeC6H4SO3H.H2O (VII.H2O), and 30 ml. C6H6 refluxed 1.5-2.0 hrs. in a Dean-Stark app., and 30 ml. C6H6 added gave 85-90% p-toluenesulfonate salts (isoPrOH-Et2O) of the following peptide esters [ester, m.p., Rf in 4:1:1 BuOH-AcOH-H2O (solvent B), and [.alpha.]26D (c, AcOH) given]: Ser-Gly-Bzl (VIII), 176.degree., 0.55, 8.2.degree. (1.7); Ser-Ala-Bzl (IX), 130.degree., 0.69, -14.3.degree.

(5.5); Ser-Glu(Bzl)2 (X), 72.degree., 0.86, -4.0.degree. (5.7). Z-Ser-Gly-Bzl (3.9 g.) refluxed 2 hrs. with 3.8 g. VII.H2O in 35 ml. C6H6 contg. 5 ml. BzlOH also gave VIII p-toluenesulfonate (XI), m. 176.degree., Rf 0.55 (B), 61% yield. To 4.2 g. XI in 30 ml. MeCN and 30 ml. THF contg. 1.4 ml. Et3N was added 3.6 g. Ia and the soln. cooled to -15.degree., treated with 2.1 g. DCCI, shaken 10 hrs. at 4.degree. and then 4 hrs. at room temp., and worked up like II to give 4.3 g. Z-.alpha.-Asp-Ser-Gly-(Bzl)2 (XII), m. 120.degree. (EtOAc), [.alpha.]26D -8.9.degree. (c 1.8, dry C5H5N), -8.0.degree. (c 6.0, AcOH); material m. 105-15.degree. with higher optical rotation ([.alpha.]26D -12.9 to -19.4.degree.) was obtained in cases where a slight excess (10%) of Et3N was used in the condensation step or when the reaction product was washed extensively with aq. NaHCO3. The optical rotation of XII (c 2% in 70:30 C5H5N-H2O) increased in 10 hrs. to a value of [.alpha.]27D -23.3 .+-. 1.0.degree. and decreased thereafter slowly. From 1.4 g. Ia, 1.7 g. IX p-toluenesulfonate, 0.66 ml. Et3N, and 0.85 g. DCCI in 50 ml. MeCN-THF was prepd., like XII, 1.9 g. Z-.alpha.-Asp-Ser-Ala-(Bzl)2 (XIII), m. 131.degree., [.alpha.]26D -17.1.degree. (c 6.0, AcOH), -20.2.degree. (c 2.0, C5H5N). The optical rotation of XIII reached a value of [.alpha.]27D -36.5.degree. within 3 hrs. at 27.degree. in 70:30 C5H5N-H2O. A sample of XIII, prepd. by the isolation procedure involving washing with aq. NaHCO3, m. 116-18.degree., [.alpha.]26.5D -21.2.degree. (c 5.9, AcOH), indicating some aspartimide formation. Strong evidence for this was obtained by phosphorylation of 1.8 g. of this material, followed by hydrogenolysis (cf. below), giving 1.05 g. product, which was resolved by anion exchange chromatography into 2 peptides with the compn. of Asp-SerP-Ala.(H2O)n. The main product (fraction D, 0.53 g.) appeared at a place in the chromatogram normal for .alpha.-aspartyl-O-phosphorylserines, and gave the normal purple ninhydrin reaction on paper chromatograms Rf 0.38 (A). The optical rotation was [.alpha.]26D -17.3.degree. (c 4.0, M HCl), and the analyses were correct for .alpha.-Asp-SerP-Ala.2H2O (XIV.2H2O). The minor component (fraction C, 166 mg.) appeared earlier in the chromatogram, indicating that it was less acidic than XIV. After isolation, it gave 1 bright yellow spot [Rf 0.44 (A)] with ninhydrin; after a year at room temp., 1 or 2 new components appeared [Rf 0.38-0.40 (A), violet color], indicating appreciable decompn. The carbonyl ir absorption band of fraction C had 2 well-sepd. peaks at 5.77 and 6.0 .mu., indicating a succinimide ring; the carbonyl ir absorption band of fraction D was broad and had the peak at 6.05 .mu.. The high optical rotation of fraction C [[.alpha.]26D -40.3.degree. (c 3.8, M HCl)] was a further indication that it was N-aspartimido-O-phosphorylserylalanine-H2O. The decompn. observed above was possibly caused by the water of hydration in opening the succinimide ring, forming a mixt. of XIV and its .beta.-isomer. Alk. phosphatase from swine kidney liberated 1 equiv. of inorg. phosphate from both fractions C and D, and at about the same rate. From 1.8 g. Ia, 2.94 g. X p-toluenesulfonate, 0.7 ml. Et3N, and 1.1 g. DCCI was prepd. like XII 3.0 g. Z-.alpha.-Asp-Ser-Glu-(Bzl)3 ester, m. 80-2.degree. (EtOAc-ligroine), [.alpha.]27D -15.2.degree. (c 1.8, dry C5H5N), [.alpha.]26D -15.2.degree. (c 5.9, AcOH); the optical rotation of this compd. reached a value of [.alpha.]27D -32.0.degree. within 3.5 hrs. in 70:30 C5H5N-H2O. From 2.8 g. V dicyclohexylamine salt (XV), 2.1 g. XI, and 1.1 g. DCCI in 80 ml. THF-MeCN was prepd. like XII 2.0 g. Z-.alpha.-Glu-Ser-Gly di-Bzl ester, m. 121.degree. (EtOAc), [.alpha.]26D -7.7.degree. (c 3.3, AcOH). From 2.76 g. XV, 2.2 g. IX p-toluenesulfonate, and 1.1 g. DCCI was prepd. like XII 2.4 g. Z-.alpha.-Glu-Ser-Ala(Bzl)2 (XVI), m. 104.degree. (EtOAc-Et2O), [.alpha.]26D -16.4.degree. (c 6.1, AcOH). VI (3.2 g.), 1.8 g. IV, and 1.1 g. DCCI in 50 ml. 1:1 THF-MeCN shaken 4 hrs. at 4.degree. and 18 hrs. at

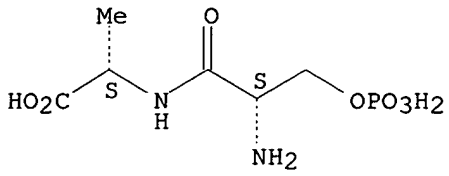
room temp., the soln. filtered and evapd., the residue treated with 150 ml. EtOAc, and the soln. filtered, washed successively with H2O, 2M HCl, H2O, and aq. NaHCO3, dried, and evapd. gave 2.9 g. XVI, m. 96-8.degree. (EtOAc-Et2O), (.alpha.)26.5D -11.2.degree. (c 6.0, AcOH). From 6.4 g. Z-Leu-Gly, 7.0 g. I, 2.8 ml. Et3N, and 4.2 g. DCCI in 100 ml. 1:1 THF-MeCN was prepd. 8.0 g. Z-Leu-Gly-Ser-Bzl, m. 128.degree. (EtOAc-Et2O), [.alpha.]26D -2.3.degree. (c 6.5, AcOH). The protected peptide (5 millimoles hydrogenated in tert-BuOH-H2O over 0.5 g. 10% Pd-C (1 equiv. HCl was added in the case of the histidine and 2 equivs. in the case of the lysine peptides), when no more H was consumed (after 0.5-2.0 hrs.) the catalyst filtered off and washed with H2O, the combined solns. evapd. in vacuo, and the residue crystd. from H2O-EtOH gave corresponding free peptide; all free peptides gave 1 spot on chromatograms in all solvent systems tested and had the normal purple ninhydrin color; they were all tested by total hydrolysis by leucine aminopeptidase or by 6M HCl; the hydrolyzates were also analyzed by paper chromatography on Whatman No. 1 paper with solvent B, 65:35 C5H5-H2O, or 10:10:5:2 BuOH-Me2CO-H2O-C5H5N. Peptide, Rf(B), Rf(A), [.alpha.]D, Temp., c in M HCl; Ser-Gly, 0.12, 0.60, 39.9.degree., 26.degree., 1.2; Ser-Ala, 0.25, 0.66, -29.5.degree., 27.degree., 1.2; Ser-Glu, 0.15, 0.62, -11.4.degree., 26.5.degree., 4.2; Ser-His, 0.03, 0.44, 14.0.degree., 26.degree., 3.9; Ile-Ser, 0.54, 0.72, 30.6.degree., 26.degree., 4.2; Asp-Ser, 0.07, 0.50, 24.0.degree., 27.degree., 1.7; Glu-Ser, 0.08, 0.46, 19.5.degree., 26.5.degree., 4.0; Lys-Ser, 0.06, 0.42, 27.9.degree., 27.degree., 3.8; Asp-Ser-Gly, 0.06, 0.47, -5.0.degree., 26.5.degree., 4.1; , , , , -8.2.degree., (c 3.2, H2O); Asp-Ser-Ala, 0.08, 0.58, -34.0.degree., 26.degree., 1.6; Asp-Ser-Glu, 0.07, 0.48, -19.5.degree., 26.5.degree., 4.0; , , , , -15.5.degree., (c 3.2, H2O); Glu-Ser-Gly, 0.09, 0.45, 8.3.degree., 27.degree., 4.4; Glu-Ser-Ala, 0.14, 0.58, 16.2.degree., 26.5.degree., 1.6; Leu-Gly-Ser, 0.34, 0.75, 36.5.degree., 26.degree., 3.9. The peptides listed in the first table were prepd. The Z-protected peptide benzyl ester (5 millimoles) was dissolved in 10 ml. dry (over BaO) C5H5N and the soln. cooled to just above the f.p. Dibenzylphosphoryl chloride (XVII), freshly prepd. from 1.9 g. dibenzyl phosphite and N-chlorosuccinimide, was added. The mixt. was shaken and kept overnight at 4.degree.. Cold EtOAc (75 ml.) and 75 ml. cold H2O were added, and the upper phase washed successively with cold H2O, M H2SO4, H2O, satd. aq. NaHCO3, and H2O, dried, and evapd. in vacuo to give phosphate triesters O,O-dibenzylphosphorylated protected serine peptides (XVIII) as solids or semisolids. When XVII was used in excess, it was possible, after long reaction times, to detect the formation of pyrophosphate and triphosphate analogs of the O-phosphorylated peptides. XVIII were hydrogenolyzed, in most cases, without further purification, although some of them may be crystd. Thus, 87% Z-glycyl(O,O-dibenzylphosphoryl)serine Bzl ester (XIX) was obtained, m. 79-80.degree. (EtOAc), Rf 0.42 [thin layer chromatography (TLC) on silica gel G with 60:40:1 ligroine-THF-AcOH (solvent C)]. Since IIIa had Rf 0.25 (C), chromatography on silicic acid may be an alternative purification procedure for XVIII and XIX. A third method for purification is the monodebenzylation procedure of Zervas and Dilaris (CA 50, 6350e). Thus, 6.5 g. XIX in 20 ml. dry Me2CO refluxed 45 min. with 1.5 g. dry NaI gave 4.3 g. diester Na salt, C27H28N2O9PNa, m. 178.degree., Rf 0.0 (TLC with C), which (3.5 g.) dissolved in 25 ml. H2O and treated with 7 ml. M HCl gave 3.3 g. IIIa O-Bzl H phosphate (XX), m. 129.degree. (EtOAc-Et2O), Rf 0.0 (TLC with C). XX (1.5 g.) treated with 0.28 g. DCCI in 15 ml. dry CH2Cl2 and after 20 min. at room temp. the soln. filtered and evapd. in vacuo gave 1.5 g. semisolid residue (XXI), Rf 0.63 (TLC with C). XXI was transformed to XX, m. 127-8.degree., Rf O (TLC with C), when left several

days in an open vessel. These facts, together with the method of synthesis, indicate XXI to be [PhCH2O2CNHCH2CONHCH(CO2CH2Ph)CH2OP(O)(OCH2Ph)]2. XVIII were hydrogenolyzed over 10% Pd-C (0.3-0.5 g./g. XVIII) in tert-BuOH-H2O as described for the prepn. of the free peptides, 1-4 hrs. shaking in a H atm. being required. The soln. filtered and evapd. in vacuo gave the phosphorylated peptide, some of which crystd. from H2O-EtOH (cf. run-on table). However, the majority of the phosphopeptides were purified by chromatography on a column of anion exchange resin, Dowex 1-X2 (formate form), as previously described (Avaeva, et al., CA 60, 12099c). The freeze-dried phosphopeptide fractions were mostly, according to analysis, in the form of monopyridinium salts. They were, therefore, triturated in H2O with a small amt. cation-exchange resin, Dowex 50 (H+ form), and the soln. filtered and again freezedried. The following paper chromatographically pure peptides were obtained in this way in 51-81% yields: [peptide, Rf(B), Rf(A); [.alpha.]D, temp., and c (M HCl)] given: SerP-Ala (H2O-EtOH), 0.09, 0.48; -16.5.degree., 26.degree., 4.2: SerP-His, 0.0, 0.27; 9.4.degree., 27.degree., 1.9: Asp-SerP, 0.03, 0.32; 21.6.degree., 27.degree., 4.2: Glu-SerP, 0.03, 0.29; 24.7.degree., 27.degree., 4.0: Ile-SerP (H2O-EtOH), 0.18, 0.62; 30.5.degree., 27.degree., 4.0: Lys-SerP, 0.03, 0.30; 25.2.degree., 25.degree., 4.0: Asp-SerP-Gly, 0.02, 0.30; -4.3.degree., 26.degree., 3.9. Asp-SerP-Ala 0.03, 0.38; -17.3.degree., 26.degree., 4.0. Asp-SerP-Glu, 0.02, 0.33; -11.2.degree., 26.degree., 4.2: Glu-SerP-Gly, 0.02, 0.35; 11.5.degree., 27.degree., 4.0: Glu-SerP-Ala, 0.04, 0.40; -4.5.degree., 25.degree., 4.3: Leu-Gly-SerP (H2O-EtOH), 0.24, 0.62; 40.6.degree., 27.degree., 4.1. Lys-SerP and SerP-His were C5H5N-free after the first freeze-drying. SerP-His was obtained by phosphorylation of N-(N-Z-Ser)-Nim-Bzl-His-Bzl. The hydrogenolysis required 12 hrs. for complete removal of the Nim-Bzl group. The procedure was used without difficulties also in the prepn. of SerP-Gly-2-14C and Gly-SerP-3-14C from glycine-2-14C and serine-3-14 C. O-Phosphoryl-DL-serine (XXII) (6.8 g.) added to a soln. (prepd. at -10.degree.) of 26 ml. SOCl2 in 100 ml. MeOH (XXII dissolved completely within 1 hr.) and the soln. evapd. in vacuo gave 7.3 g. XXII Me ester (XXIII), m. 198.degree. (decompn.) (H2O-MeOH), Rf 0.19 (B), 0.55 (in 80:20 PhOH-H2O, identical (mixed m.p., Rf values, and ir spectrum) with XXIII prepd. (CA 53, 22157f) by hydrogenolysis of N-Z-(O,O-diphenylphosphoryl)-DL-serine Me ester. O-Phosphorylserine (4.7 g.) treated similarly gave 3.7 g. corresponding optically active Me ester, m. 167.degree. (decompn.), [.alpha.]26D 12.0.degree. (c 4.3, M HCl), Rf 0.19 (B). Threonine (29 g.; [.alpha.]26D -14.4.degree. (c 2.1, 5N HCl)) treated with chlorophosphoric acid as described for serine (CA 53, 22157f) and after hydrolysis EtOH and Et2O added gave 22.8 g. O-phosphorylthreonine (XXIV), m. 189.degree. (decompn.) (H2O-EtOH), [.alpha.]27D --7.9.degree. (c 2.5, H2O), Rf 0.11 (B), 0.46 (A), 0.03 (in 35:35:30 C5H5N-iso-AmOH-C2O), the m.p. and [.alpha.]D being in accord with those of XXIV isolated by Verdier (CA 47, 5971b) from an acid hydrolyzate of bovine casein. The acid hydrolyzate (20 hrs., 110.degree., sealed tubes) of synthetic XXIV (38.7 mg. in 2200.1 mg. 5M HCl) had negligible optical rotation, [.alpha.]26D -1.5.degree.. Paper chromatographic analysis of the hydrolyzate indicated threonine to be the main product present. In addn., a small amt. unchanged XXIV was present. Little loss of optical activity was observed when threonine was heated similarly in 5M HCl (41.4 mg. in 2167.0 mg.; [.alpha.]26D -13.2.degree. (c 1.7)). When H3PO4 (24.5 mg. 85% H3PO4 was present during the hydrolysis of threonine (40.0 mg. in 1987.6 mg. 5M HCl), the rotation became [.alpha.]26D -12.8.degree. (c 1.8).

IT **6403-04-9**, Alanine, N-L-seryl-, dihydrogen phosphate (ester), L- (prepn. of)

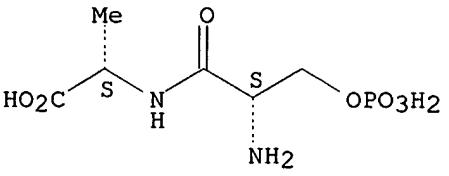
RN 6403-04-9 HCAPLUS
CN Alanine, N-L-seryl-, dihydrogen phosphate (ester), L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1966:28766 HCAPLUS
DOCUMENT NUMBER: 64:28766
ORIGINAL REFERENCE NO.: 64:5369f-g
TITLE: Hydrolysis of phosphopeptides. III. The action of alkaline phosphatase preparations from kidney, bone, and yeast on O-phosphorylated model compounds
AUTHOR(S): Csopak, Hedvig; Folsch, Georg; Strid, Lars; Mellander, Olof
CORPORATE SOURCE: Univ. Goteborg, Swed.
SOURCE: Acta Chem. Scand. (1965), 19(7), 1575-82
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. preceding abstr. Swine kidney, calf bone, and yeast phosphatase enzymes were prepd. and the rate of PO43- liberation from 30 phosphopeptides was detd. The enzymes were not purified sufficiently to exclude the possibility of the presence of enzymes other than phosphatases. Position of the PO43- affected the rate of hydrolysis. It was faster when in the N-terminal position than when in the reversed sequences. The ext. from the kidney tissue was more active than that from bone tissue. The ext. from yeast caused hydrolysis in 10 peptides. 21 references.
IT **6403-04-9**, Alanine, N-L-seryl-, dihydrogen phosphate (ester), L-
6665-27-6, Leucine, N-L-seryl-, dihydrogen phosphate (ester), L-
6665-42-5, Glycine, N-L-seryl-, dihydrogen phosphate (ester)
(hydrolysis by phosphatase)
RN 6403-04-9 HCAPLUS
CN Alanine, N-L-seryl-, dihydrogen phosphate (ester), L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6665-27-6 HCAPLUS
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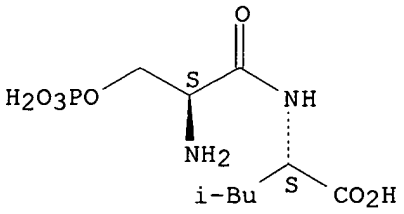
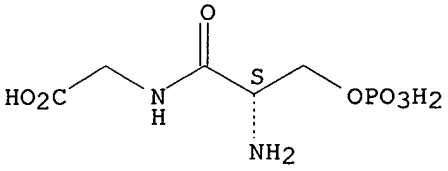
Absolute stereochemistry.



RN 6665-42-5 HCAPLUS
CN Glycine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1966:28765 HCAPLUS
DOCUMENT NUMBER: 64:28765
ORIGINAL REFERENCE NO.: 64:5369c-f
TITLE: Hydrolysis of phosphopeptides. II. Leucine aminopeptidase hydrolysis of free and O-phosphorylated serine peptides
AUTHOR(S): Folsch, Georg; Strid, Lars; Mellander, Olof
CORPORATE SOURCE: Univ. Goteborg, Swed.
SOURCE: Acta Chem. Scand. (1965), 19(7), 1566-74
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. CA 56, 6083i; following abstr. The relative rate of hydrolysis by leucine aminopeptidase (I) of substrates consisting of phosphate-free peptides (II), O-phosphorylated (III), O-monophenylphosphorylated (IV), and O-pyrophosphorylated serine peptides (V) was detd. The enzyme hydrolyzed peptides having N-terminal O-phosphorylserine only about 0.4% as fast as the corresponding nonphosphorylated peptides. Dipeptides with O-phosphorylserine in the C-terminal position were hydrolyzed approx. 1% as fast as were the corresponding serine peptides with a free hydroxyl group. The hydrolysis rate was directly proportional to the distance of the PO43- group from the free .alpha.-amino end. A pyrophosphoryl group retarded hydrolysis even more than a simple PO43- group. The attachment of a hydrophobic benzene ring to the PO43- group increased the rate of hydrolysis to the same or even higher value than that of the nonphosphorylated analogs. Percent hydrolysis in 20 min., using 0.1% of I, varied from 20.0 to 0.01 for the 15 II tested, 7.4 to 0.001 for 11 III tested, 0.58 to 0.04 for the 2 IV, and 0.055 to 0.003 for the 2 V substrates. Compds. tested for hydrolysis from the highest to the lowest rate in each group were: II, L-Leu-Gly, L-Leu-L-Ser, L-Leu-Gly-L-Ser, L-Ser-L-Leu, L-Ile-L-Ser, Gly-L-Leu, .alpha.-L-Glu-L-Ser-L-Ala,

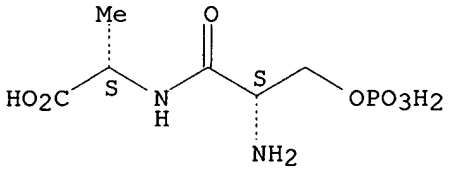
L-Lys-L-Ser, L-Ser-Gly, DL-Ser-Gly, L-Ser-L-Ala, Gly-DL-Ser, .gamma.-L-Glu-L-Ser, Gly-Gly, and .alpha.-L-Glu-L-Ser; group III, L-Leu-Gly-SerP, L-Leu-SerP, L-SerP-L-Leu, L-Ile-L-SerP, L-Lys-L-SerP, L-SerP-L-Ala, DL-SerP-Gly, Gly-DL-SerP, L-SerP-L-SerP, and .gamma.-L-Glu,L-SerP; group IV DL-Ser.vphi.P-Gly, and Gly-DL-Ser.vphi.P; and group V L-Leu-L-SerPP, and L-SerPP-L-Leu. The above P represents O-phosphorylated, the .vphi.P O-monophenylphosphorylated, and PP O-pyrophosphorylated. 29 references.

IT **6403-04-9**, Alanine, N-L-seryl-, dihydrogen phosphate (ester), L-
6665-27-6, Leucine, N-L-seryl-, dihydrogen phosphate (ester), L-
6665-32-3, Glycine, N-DL-seryl-, dihydrogen phosphate (ester)
(hydrolysis by leucine aminopeptidase)

RN 6403-04-9 HCAPLUS

CN Alanine, N-L-seryl-, dihydrogen phosphate (ester), L- (8CI) (CA INDEX NAME)

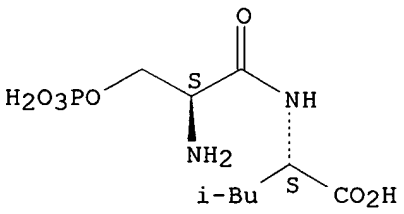
Absolute stereochemistry.



RN 6665-27-6 HCAPLUS

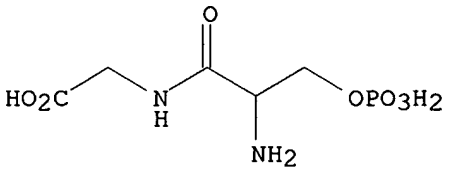
CN L-Leucine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6665-32-3 HCAPLUS

CN Glycine, N-DL-seryl-, dihydrogen phosphate (ester) (8CI) (CA INDEX NAME)



L19 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1965:455686 HCAPLUS

DOCUMENT NUMBER: 63:55686

ORIGINAL REFERENCE NO.: 63:10199a-b

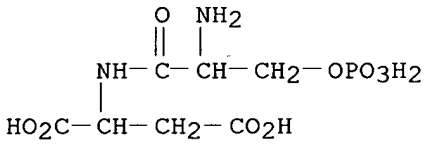
TITLE: Phosphopeptides. Synthesis and enzymic studies
AUTHOR(S): Koehn, Paul V.; Kind, C. Albert
CORPORATE SOURCE: Univ. of Connecticut, Storrs
SOURCE: Arch. Biochem. Biophys. (1965), 111(3), 614-18
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Phosphoprotein phosphatase obtained from chick embryo readily dephosphorylates casein which is characterized by sequences of O-phosphorylserine residues and by a high content of glutamic acid and aspartic acid. Dipeptides incorporating these amino acids and (SerP)3 were synthesized. The phosphopeptides, equivalent to 380 .gamma. P in acetate buffer (pH 5.8). were dephosphorylated by acid phosphatase but not by phosphoprotein phosphatase. Possible min. structural features of a peptide required for phosphoprotein phosphatase activity are discussed.

IT **3785-84-0**, Aspartic acid, N-seryl-, dihydrogen phosphate (ester)
(prepn. and diphosphorylation of)

RN 3785-84-0 HCAPLUS

CN Aspartic acid, N-seryl-, dihydrogen phosphate (ester) (8CI) (CA INDEX NAME)



L19 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1963:60714 HCAPLUS
DOCUMENT NUMBER: 58:60714
ORIGINAL REFERENCE NO.: 58:10423a-c
TITLE: Calcium, magnesium, and manganese(II) complexes of some O-phosphorylated peptides
AUTHOR(S): Osterberg, Ragnar
CORPORATE SOURCE: Univ. Goteborg, Swed.
SOURCE: Acta Chem. Scand. (1962), 16, 2434-51
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Complex formation between Ca, Mg, and Mn(II) ions and O-phosphorylated ethanolamine, seryllysine, serylglycine, glycylserine, glycylserylglycine, and serylglutamic acid was studied by pH titration at 25.degree. in a medium contg. const. Cl- concn. Complexes of the type MpHqA were formed where p:q = 1:1 and 1:0 for the first two ligands, p:q = 1:1, 1:0, and 2:0 for the next three ligands (although p:q = 2:0 was not measurable for M = Ca++), and p:q = 1:2, 1:1, 1:0, 2:1, and 2:0 for the last ligand. Stability consts. for all indicated complexes were tabulated and the coordination sites discussed. The observed differences between Ca++ and Mg++ in complexing ability was correlated to ionic size. The definitely greater tendency of Mg++ and Mn++ ions to dinuclear complex formation compared with Ca++ was discussed in relation to the specificity of enzymes for these ions.

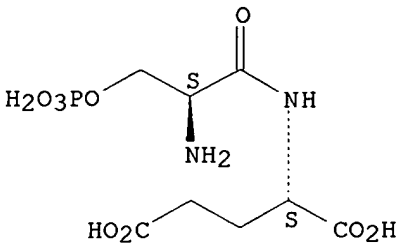
IT **93115-01-6**, Hydrogen [N-L-seryl-L-glutamic acid phosphato(4-)]magnesate **93168-28-6**, Hydrogen [N-L-seryl-L-glutamic acid phosphato(4-)]calciate **93285-19-9**, Hydrogen [N-DL-serylglycine phosphato(3-)]calciate **93409-37-1**,

Hydrogen [N-L-seryl-L-glutamic acid phosphato(3-)]aquocalciate **93440-75-6**, Manganese, [(N-L-seryl-L-glutamic acid phosphato(4-)]tetraaquodi- **93481-54-0**, Calcium, [N-L-seryl-L-glutamic acid phosphato-(4-)] tetraaquodi- **93784-32-8**, Magnesium, [N-L-seryl-L-glutamic acid phosphato(4-)]tetraaquodi- (prepn. of)

RN 93115-01-6 HCAPLUS

CN Hydrogen [N-L-seryl-L-glutamic acid phosphato(4-)]magnesate (7CI) (CA INDEX NAME)

Absolute stereochemistry.

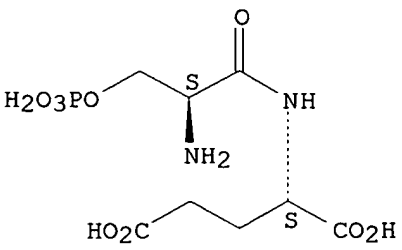


● Mg

RN 93168-28-6 HCAPLUS

CN Hydrogen [N-L-seryl-L-glutamic acid phosphato(4-)]calciate (7CI) (CA INDEX NAME)

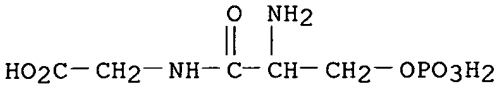
Absolute stereochemistry.



● Ca

RN 93285-19-9 HCAPLUS

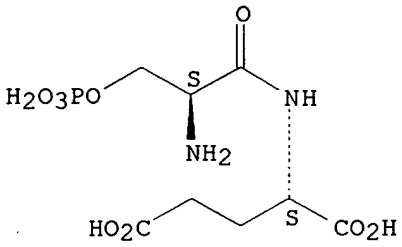
CN Hydrogen [N-DL-serylglycine phosphato(3-)]calciate (7CI) (CA INDEX NAME)



● Ca

RN 93409-37-1 HCAPLUS
CN Hydrogen [N-L-seryl-L-glutamic acid phosphato(3-)]aquocalciate (7CI) (CA INDEX NAME)

Absolute stereochemistry.

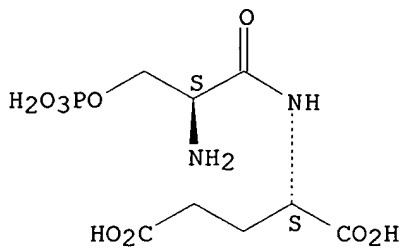


● Ca

● H_2O

RN 93440-75-6 HCAPLUS
CN Manganese, [N-L-seryl-L-glutamic acid phosphato(4-)]tetraaquodi- (7CI) (CA INDEX NAME)

Absolute stereochemistry.

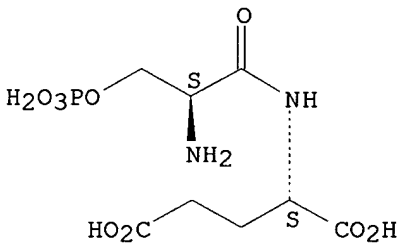


●2 Mn(II)

●4 H_2O

RN 93481-54-0 HCAPLUS
CN Calcium, [N-L-seryl-L-glutamic acid phosphato(4-)]tetraaquodi- (7CI) (CA INDEX NAME)

Absolute stereochemistry.

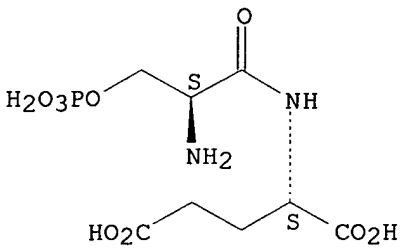


●2 Ca

●4 H_2O

RN 93784-32-8 HCAPLUS
CN Magnesium, [N-L-seryl-L-glutamic acid phosphato(4-)]tetraaquodi- (7CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 Mg

●4 H_2O

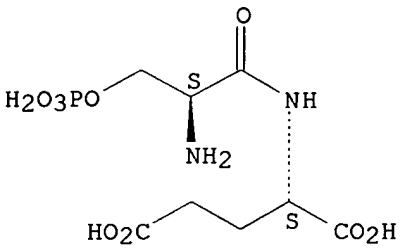
L19 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1963:60713 HCAPLUS
DOCUMENT NUMBER: 58:60713
ORIGINAL REFERENCE NO.: 58:10422h,10423a
TITLE: Biosynthesis of amino sugar in hyaline cartilage
AUTHOR(S): Seno, Nobuko
CORPORATE SOURCE: Ochanomizu Univ., Tokyo
SOURCE: Seikagaku (1962), 34, 629-31
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB An enzyme to synthesize amino sugar from glucose 1-phosphate and glutamine was prepd. from hyaline cartilage tissues. The optimum pH of the reaction was 7.4, the same as rat liver enzyme. An (NH4)2SO4 pptg. fraction at higher than 2.3M showed the highest enzyme activity, whereas a fraction pptg. at 1.7-2.3M satn. was the most active for rat liver enzyme. Enzyme activity (amino sugar formation micromoles/mg. enzyme protein N) of hyaline cartilage was about 2.5 times higher than that of rat liver.

IT **93168-28-6**, Hydrogen [N-L-seryl-L-glutamic acid phosphato(4-)]calciate **93285-19-9**, Hydrogen [N-DL-serylglycine phosphato(3-)]calciate **93409-37-1**, Hydrogen [N-L-seryl-L-glutamic acid phosphato(3-)]aquocalciate
(prepn. of)

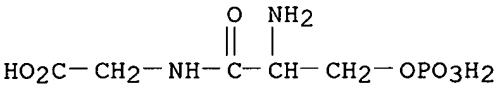
RN 93168-28-6 HCAPLUS
CN Hydrogen [N-L-seryl-L-glutamic acid phosphato(4-)]calciate (7CI) (CA INDEX NAME)

Absolute stereochemistry.



● Ca

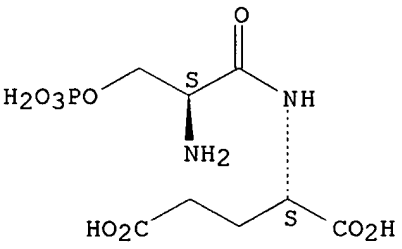
RN 93285-19-9 HCAPLUS
CN Hydrogen [N-DL-serylglycine phosphato(3-)]calciate (7CI) (CA INDEX NAME)



● Ca

RN 93409-37-1 HCAPLUS
CN Hydrogen [N-L-seryl-L-glutamic acid phosphato(3-)]aquocalciate (7CI) (CA INDEX NAME)

Absolute stereochemistry.



● Ca

● H_2O

L19 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1962:42074 HCAPLUS

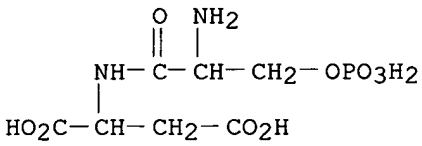
DOCUMENT NUMBER: 56:42074
ORIGINAL REFERENCE NO.: 56:7975a-c
TITLE: Separation of O-phosphorylated amino acids and peptides on anion exchange resin
AUTHOR(S): Strid, Lars
CORPORATE SOURCE: Univ. Goteborg, Swed.
SOURCE: Acta Chem. Scand. (1959), 13, 1787-90
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The following compds. were sepd. on a 1.6 .times. 50-cm. anion-exchange column contg. Dowex 1-X2(Cl-), 200-400 mesh: O-phosphorylserine, O-phosphorylthreonine, glycyl-(O-phosphoryl)serylglycine, glycyl-(O-phosphoryl)serine, leucyl-(O-phosphoryl)serine, O-phosphorylseryl-(O-phosphoryl)serine, and O-phosphorylserylglycine, -leucine, -aspartic acid, and -glutamic acid. By slowing passing 2M HCO2Na, pH 5.5, through the column until the effluent gave a neg. Cl- test, the resin was converted to the formate. Phosphorylated amino acids and phosphopeptides contg. neutral amino acids are eluted within a narrow region, the order of elution agreeing with the pK value of the CO2H group.

IT **3785-84-0**, Aspartic acid, N-seryl-, dihydrogen phosphate (ester) (chromatography of)

RN 3785-84-0 HCAPLUS

CN Aspartic acid, N-seryl-, dihydrogen phosphate (ester) (8CI) (CA INDEX NAME)



L19 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1962:38740 HCAPLUS
DOCUMENT NUMBER: 56:38740
ORIGINAL REFERENCE NO.: 56:7418e-i
TITLE: Synthesis of phosphopeptides. II. O-Phosphorylated dipeptides of L-serine
AUTHOR(S): Folsch, George
CORPORATE SOURCE: Univ. Gotheeburg, Swed.
SOURCE: Acta Chem. Scand. (1959), 13, 1407-21
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. CA 53, 17919h.-Diphenyl- and dibenzylphosphoryl chlorides phosphorylated 6-(N-carbobenzoxy)dipeptide benzyl esters of L-serine with amino acid sequences found in phosphoproteins; catalytic hydrogenolysis of the dibenzylphosphoryl derivs. gave pure phosphopeptides, while the diphenylphosphoryl analogs frequently gave partially hydrogenated derivs. Compds. prepd. include the following L,L-N-carbobenzoxy dipeptide benzyl esters (compd., % yield, and m.p. given, Z = PhCH2OCO): Z-ser-glu-OCH2Ph, 78, 125.degree.; Z-ser-asp-OCH2Ph, 89, 128-9.degree.; Z-ser-leu-OCH2Ph, 90, 83-4.degree.; Z-ser-ser-OCH2Ph, 71, 138-9.degree.; Z-glu-ser-OCH2Ph, 76, 127;; and Z-leu-ser-OCH2Ph, 86, 122-3.degree.. The following dipeptides of L-serine [compd., % yield, and [.alpha.]21D (N HCl, l 1) given]: H-ser-glu-OH, 82, -10.8.degree. (c 4.4); H-ser-asp-OH, 78,

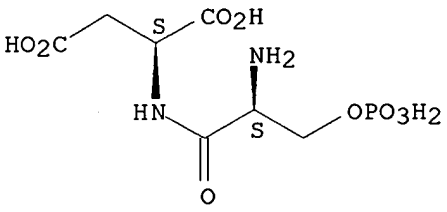
1.5.degree. (c4.0); H-ser-leu-OH, 79, -18.8.degree. (c 2.4); H-ser-ser-OH, 74, 14.8.degree. (c 6.4); H-glu-ser-OH, 80, 29.0.degree. (c 5.1); and H-leu-ser-OH, 74, 27.8.degree. (c 6.9). The following dipeptides of O-phosphoryl-L-serine [compd., % yield, and [.alpha.]21D (N HCl, l 1) given; ser P = NHCH[CH2OPO(OH)2]CO]; H-ser-P-glu-OH (I), 53, -9.5.degree. (c 4.2); H-ser-P-asp-OH, 62, -2.2.degree. (c 2.7); H-ser-P-leu-OH, 64, -16.0.degree. (c 4.0); H-ser-P-ser-OH, 57, 8.2 (c 4.7); H-glu-ser-P-OH, 54, 23.3.degree. (c 4.4); and H-leu-ser-P-OH, 62, 24.5.degree. (c 7.0). The following dibenzyl, di-Ph, and Ph phoshorylated derivs. (compd., % yield, and m.p. given): Z-ser[OPO(OCH2Ph)2]-gly-OCH2Ph, 75, 104-5.degree.; Z-gly-ser[OPO(OCH2Ph)2]-OCH2Ph, 76, 81-2.degree.; Z-ser[OPO(OPh)2]-asp-(OCH2Ph)2, 93, 62-3.degree.; Z-glu(OCH2Ph)ser[OPO(OPh)2]-OCH2Ph, 90, 75-6.degree.; H-ser[OPO(OPh)2]-glu(OH)2, 48, 182-5.degree. (decompn.); H-ser[OPO(OPh)OH]-glu(OH)2, 21, 174-8.degree. (decompn.); H-ser[OPO(OPh)OH]-asp(OH)2, 28, 167-71.degree. (decompn.); and H-ser[OPO(OPh)-OH]-leu-OH, 11, 202-4.degree. (decompn.). Also prepd. were H-ser[OPO(OPr)2OCH2Ph], m. 130-1.degree. (decompn.), the brucine salt of I, m. 171-3.degree. (decompn.), and the PhSO3H, p-MeC6H4SO3H, and HCl salts of L-serine benzyl ester, m. 110-12.degree., 94-5.degree., and 172-4.degree., [.alpha.]21D -4.1.degree. (MeOH, c4.4, l 1), resp.

IT **1492-20-2**, Aspartic acid, N-L-seryl-, dihydrogen phosphate (ester), L- **6665-27-6**, Leucine, N-L-seryl-, dihydrogen phosphate (ester), L-
(prepn. of)

RN 1492-20-2 HCAPLUS

CN L-Aspartic acid, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6665-27-6 HCAPLUS

CN L-Leucine, N-(O-phosphono-L-seryl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.